Clinical Medicine

Original Articles for November, 1958

EDITORIAL

Our Own Cravings as Reliable Guides

It is surprising that so many persons survived the superstitious practices that formerly governed medical treatment

JAMES M. NORTHINGTON, M.D., *Editor*

We are getting away from the dominance of the "original sin" concept. Walking barefooted on hot irons, lying on a bed of thorns, wearing sharp pebbles in the shoes and a camel's hair shirt next to the skin, fasting, refusing to molest our body vermin, refraining from bathing—all of these practices had their origin in the idea that it was sinful to be comfortable, and its corollary that torturing oneself was an act of piety and grace. All of these have about gone out, and it is to be noted that there has been an almost regular mitigation in severity.

Some persons who are now living can remember when it was the orthodox medical practice to deny cold water to a patient burning with fever, and certainly this was a holdover from the priest-doctor era—a product of the "reasoning" that man being inherently wicked, all his natural cravings are bad for himself as well as for others. In contrast with this demoniac teaching, the American Indian not only gave cold water to those with fever, but bathed them frequently with it. This practice was observed by members of one of the earliest European expeditions to touch on the shores of what is now North Carolina, and the historian expresses great wonder that "many so treated recover."

Now it seems that it is about to be conceded by doctors in general, and we hope accepted by the laity, that

our appetites for food are about 90 per cent trustworthy as to quality, quantity and spacing. A good many of us have long contended that our internal economy had arranged automatic alarms to serve notice on us when we needed water, rest, sleep, fats, proteins, carbohydrates, mineral salts, or vitamins. Our own opinion is that if each person in one group were restricted for a year to a menu prescribed by the ablest doctors in the world in every particular—as to kind, method of preparation, time taken for eating and time between meals; and, through that same year, the people of another group of equal size were to follow the immemorial custom of being governed largely by appetite and available supply, the end of the year would find many more healthy persons in the latter than in the former group.

An experiment[1] with newly-weaned infants indicated that such children choose with remarkably good results from a wide range of commonly used food materials, served unseasoned and, when cooked at all, only in the simplest manner.

The experiment amazed the observer by the selections made as to kind, quantity and variety, since it was such as to maintain themselves at their very best. The evidence is in favor of a wide range, and for allowing glands and red meats to children who desire these foods.

Recollections of my own childhood are clear on the point of being allowed to eat raw potatoes, turnips and cabbage stalks freely, go in swimming during dog-days, and otherwise defy the superstitions as to health which caused some of our playmates to be denied much happiness. And it was noted on a recent visit that two of them had lost all their teeth.

Some few persons, perhaps five per cent, need to have diets prescribed. For the ninety-five, dieting, other than that which experience has taught each one, is mostly humbug.◀

1. Davis, Clara M., *A.M.A. Am. J. Dis. Child.*, 36: 651,1928.

The Doctor's Whole Duty

If we may properly act on the assumption that man is something more than a completely determined animal, an important conclusion about medical practice follows. The relationship between doctors and their patients is deeper than that entailed by the solution of scientific and measurable problems. It is in truth a personal relationship in which intuition, sympathy, and compassion play a great part. To avoid misunderstanding, let us acknowledge that most of the manifest achievements of recent years have been due to distinguished work in basic and clinical science, and that it is our responsibility to encourage all such work and to accept its verified conclusions. But we must never forget the large part of clinical practice which depends on qualities that science cannot yet measure and possibly never will.

Our duty is clear. We have to put at the service of the patient, when it is necessary, all the resources of scientific investigation and treatment. But in addition we have to maintain in him the personal interest and concern of a friend.

Thomson, A. P., *Brit. M.J.*, 2:119-121,1958.

ORIGINAL ARTICLE

Physical Medicine in the Treatment of Patients With Myocardial Infarction

Some recommendations are made for the physical rehabilitation of the patient with myocardial infarction

IGHO HART KORNBLUEH, M.D.,* EUGENE MICHELS, B.S.,* and SAMUEL BAER, M.D., F.A.C.P.,† *Philadelphia, Pennsylvania*

Great progress has been made in the diagnosis and treatment of what is popularly called "a heart attack." It is surprising how many aspects of the management of this condition are unsettled. When can a patient with myocardial infarction brush his teeth, use a commode, shave himself? When can he feed himself, watch television, take a shower, resume normal family life, etc.? The supervision of the physical, social and economic adjustments that are necessary demands the highest skill of the responsible physician.

It is in an attempt to clarify some of these uncertainties in the handling of a patient with acute myocardial infarction that this article has been written. Many of these recommendations may not meet with general approval; some need to be modified from patient to patient. Certain it is, however, that attention has been called to a portion of the treatment of acute myocardial infarction that is often hastily considered or overlooked entirely.

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GENERAL CONSIDERATIONS

There is a distinctive trend against prolonged bedrest and enforced inactivity. Mounting evidence[1,2] favors a more liberal approach. The armchair treatment[3] offers perhaps less comfort but a greater freedom of movement for the patient, thus promoting more physical activity with improved sleep, appetite, elimination, and mental outlook, as well as preventing contractures, atrophies, shoulder-hand syndromes, and thrombo-embolic episodes.

The majority of patients kept in the daytime at absolute rest perform in sleep a great variety of movements of all four extremities and twisting and bending of the trunk, without any apparent ill effects. The great amount of care and attention needed during the long convalescence from acute cardiac episodes can be reduced substantially by permitting self-feeding, use of a bedside commode, and other limited activities.

Improvement is effected in somatic and psychic symptoms. An elastic program of exercises and activities of daily living[4] adaptable to individual needs counteracts the monotony and helps in combating the anxiety, frustration, and depression based on realization of the gravity of the condition and the future social and economic consequences. Physical activity, even in this limited scope, plays a significant part in restoration of the patient's confidence and in his final recovery.

CONVALESCENCE

Convalescence from an acute myocardial infarction can be divided into three distinctive stages:

1. Period of absolute rest.
2. Gradual initiation of activities and bedside exercises ending with the ambulation of the patient.
3. Full rehabilitation with the goal of normal and productive life.

This program deals only with the second stage. The third phase[5] comprises rehabilitation measures designed especially for prevention of permanent invalidism and conditioning for resumption of normal life and work within the limits of cardiac tolerance.

PHYSICAL ENVIRONMENT

More attention must be directed towards the physical environment in which the convalescent spends weeks or months. Optimum room temperature, air flow, and humidity are helpful in minimizing the circulatory stress aggravated by extremes of the microclimate.

In hot zones or during the summer months an air conditioning unit promotes the comfort and well-being of the patient. Recent studies point towards a favorable influence of artificial ionization of the air on a number of conditions. The addition of an equalizing ion generator will reduce dust, re-establish natural outdoor conditions, and increase the value of a controlled climate in the sick room.

ENERGY REQUIREMENTS

Exercises based on energy expenditures must consider all somatic, psychic, social and environmental aspects, and incorporate these findings into a personalized program. For maximum benefits and a minimum of exertion, the scope, frequency, number, speed, and duration of each

1. Benton, J. G., et al., *J.A.M.A.*, 144:1443-1447, 1950.
2. Hellerstein, H. K., & Ford, A. B., *J.A.M.A.*, 164: 225-231,1957.
3. Levine, S. A., & Lown, B., *J.A.M.A.*, 148:1365-1369,1952.
4. Kornblueh, I. H., and Michels, E., *Pennsylvania M.J.*, 60:1575-1578,1957.
5. Cardiovascular Rehabilitation, Edited by White, P., et al., The Blakiston Division, McGraw-Hill Book Company, Inc., New York, London, 1957.

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Chapman, L. E.: J. Am. Geriatrics Soc. 6:269, 1958

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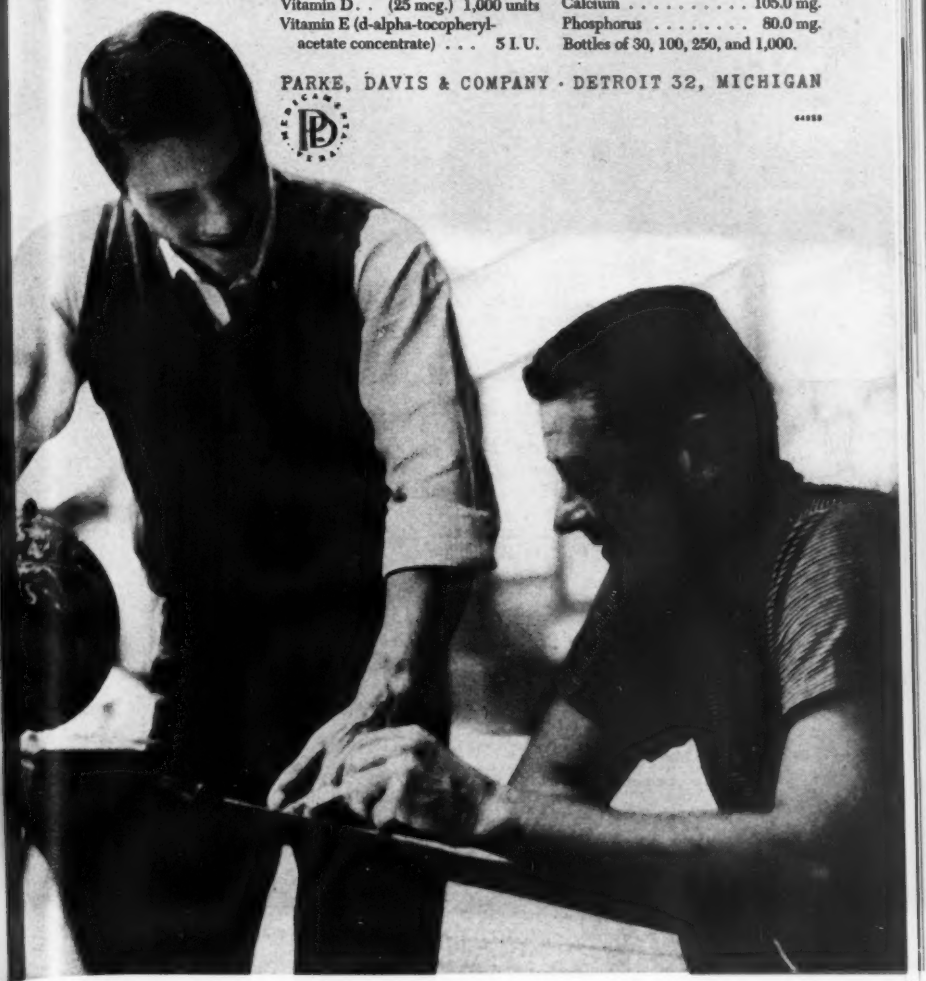

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1959, p. 683

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TABLE OF APPROXIMATE ENERGY REQUIREMENTS FOR HEALTHY PERSONS (ADJUSTED) [6-10]

Position and Activity	Cal/min.
Supine (basal)	.98 - 1.17
Lying (at ease)	1.1 - 1.4
Sitting (at ease)	1.1 - 1.6
Sitting (writing)	1.90 - 2.1
Sitting (reading)	1.98
Standing (at ease)	1.5 - 1.9
Conversation (lying)	1.4
Use of bedpan	4.7
Use of bedside commode	3.6
Passive exercises in recumbent position	1.5 - 2.5
Washing hands - face, brushing hair	2.5 - 3.3
Washing and shaving	2.6
Washing, dressing, shaving	3.8
Walking slowly indoors 2.4 mph.	3.6 - 4.3
Walking up and down stairs (97/min.)	8.4
Driving a car (slowly)	2.8
Bicycling 5.5 mph. on level ground	4.5
Peeling potatoes	2.7
Washing dishes	3.3
Copper tooling (sitting)	1.8
Hand sewing (sitting)	1.3 - 1.7
Knitting (sitting)	1.3 - 1.7
Hand loom weaving (sitting)	1.9
Chip carving (reclining)	2.0
Leather carving (sitting)	1.65

type of exercise also requires individual consideration.

No intolerable physical exertion has been shown to result from basic self care activities. In contrast to emotional tensions and restlessness, light activities involving the use of hands and forearms increase the cardiac output very little. It is important to differentiate between cardiac output and energy requirements as there is considerable variation between these.

The energy requirements noted in Table 1 serve only as a general rule. Age, sex, weight, fear, pain, and the climate of the sick room alter the metabolic cost of all activities.

The time schedule is determined from the date of the coronary occlusion. The exercise and activities program is governed by the general condition of the patient. Close cooperation of the physiatrist and the physical therapist with the attending physician is of paramount importance. All active exercises should be executed very slowly with frequent rest periods. The patient must be carefully watched for signs of cardiac and circulatory distress.

EXERCISE PROGRAM*

First Week

Absolute bedrest

Second Week

1. Light passive exercises of both upper extremities within the complete range of motion of each joint. These are executed entirely by the physical therapist with no active ef-

6. Passmore, R., & Durnin, J. V. G. A., *Physiol. Rev.*, 35:801-840,1955.
7. Gordon, E. E., *Medical Science*, 3:16-20,1958.
8. Gordon, E. E., *Modern Medicine*, 25:83-91,1957.
9. Kottke, F. J., et al., *Postgraduate Med.*, 23:533-544,1958.
10. Handbook of Biological Data, Edited by Spector, W. S., W. B. Saunders Company, Philadelphia, London, pp. 347-349, 1956.

*The authors are indebted to the editors of the *Pennsylvania Medical Journal* for the permission to use parts of our article published in the December, 1957 issue.

fort on the part of the patient:

Shoulder flexion and extension
Internal rotation and external rotation
Abduction and adduction
Forearm pronation and supination
Elbow flexion and extension
Abduction and adduction
Wrist flexion and extension
Flexion and extension of fingers
Abduction and adduction of fingers

Frequency: One time each during the first two days, two times each during the third and fourth days, etc., increasing the number of repetitions by one every two days.

2. Light active exercises to both lower extremities performed by the patient with some assistance from the therapist. The following are performed one time each on the first two days, with an increase of one repetition added every two days:

Quadriceps setting
Gluteus maximus setting
Internal and external rotation of lower extremity
Inversion and eversion of ankle
Ankle dorsiflexion and plantar flexion
Flexion and extension of toes

3. Use of bedside commode with full assistance rendered by another person.

THIRD WEEK

1. Continuance of exercises as outlined previously.

2. Active motions of the neck one time each the first day with an increase of one repetition per day.

Rotation of head and neck to left and right
Lateral flexion of head and neck to left and right
Diaphragmatic breathing exercises, once at each period, increasing subsequently by one repetition per day to a maximum of five, twice daily
Slow, supported rolling in bed from one side to another

3. Self feeding should be encouraged gradually over a period of seven or eight days.

FOURTH WEEK

1. Change passive to light active exercises. Let the patient perform each of the above-mentioned upper extremity motions actively with no assistance from the therapist. Begin with one complete motion and progress by one repetition per day.

2. Active exercises for the lower extremities:

Combined hip and knee flexion, then extension to rest position
Knee extension from a position of hip and knee flexion with support under the knee
Hip abduction and adduction
Straight leg raise, one at a time

3. Diaphragmatic breathing exercises according to tolerance.

4. Washing of face and hands by the patient.

5. Shaving.

6. Dangling or sitting up over side of bed with help of the therapist, with feet supported on a chair.

In this transitional phase of convalescence the use of a tilt table for effortless standing is very helpful.

FIFTH WEEK

1. Continue exercise regimen with a maximum of 10 repetitions for any one exercise.

2. Sitting in a chair.

3. Standing (unsupported).

4. Walking indoors with a gradual increase in distance depending upon the patient's tolerance, stabilization of the electrocardiogram, and normalization of the blood sedimentation rate.

5. Use of bathroom on the same floor.

FROM SIXTH WEEK ON

1. Exercises and walking should be continued.

2. Increased scope of self-care activities.

3. Training in ascending and descending stairs, starting with two steps and increasing by two every day to a total of 16 steps after one week. Chair patients follow a similar schedule. However, they may stand up after three weeks and walk after four weeks.

Occupational therapy may be added at the end of three weeks. It should be interesting, but neither physically nor mentally tiresome, and include teaching the patient non-exerting techniques of daily activities in accordance with his cardiac status.

CONTRAINDICATIONS

1. Cardiac distress
2. Cardiovascular failure
3. Persistent arrhythmias
4. Fever
5. Dyspnea
6. Palpitations
7. Periods of rest and sedation

SUMMARY

The place of physical medicine in the prevention of complicating sequelae of prolonged bed rest and a program of supervised therapeutic exercise and activities for patients recovering from a myocardial infarction has been presented.◀

Coronary Heart Disease in India

Western writers seem to believe that the "material civilization" of the West is responsible for the increased incidence of this disease in their countries and that Asiatics are far less prone to fall victim to this malady. The presented data indicate that coronary disease forms a big group in the cardiac population of India, and, whereas several of the etiological factors observed run true to description by Western authors, there are some local factors that may provide material for further thought.

The patients were divided into three classes:

1. Patients from well-to-do and professional classes.

2. The middle class—clerks, schoolteachers, shopkeepers, more prosperous farmers.

3. Laborers, factory workers, poor farmers, small shopkeepers, etc. The tabulation shows that 91 per cent of the cases came from the upper and middle classes. One cannot draw any conclusion, for the obvious reason that these seek medical advise readily. People who had to earn their living by hard physical activity formed a negligible proportion in this series, but these were less likely to seek medical advice readily.

Coronary disease is a major cause of mortality in countries that are materially more advanced. Those in India at present must continue to think in terms of more important problems —those of infant mortality, infectious diseases, nutritional disorders, overpopulation, and a host of other public health problems. With the present standard of vital statistics it is difficult to give the true incidence of coronary disease in this part of the world. But with coronary disease accounting for 28.4 per cent of our 3,054 cardiac cases, it is difficult to share the view held by some Western writers about coronary disease being uncommon in materially less favored countries.

Malhotra, R. P., & Pathania, N. S., *Brit. M.J.*, 2:528-531,1958.

ORIGINAL ARTICLE

Asthma, Bronchitis, Rhinitis and Sinusitis: Adjunctive Treatment With Intramuscular Chymotrypsin

Sixty patients were given chymotrypsin as adjunctive therapy with good clinical results

D. J. PARSONS, M.D., F.A.C.A., *Springfield, Ohio*

Clinical experiences with inhalation[1,2,3] and topically applied[4] trypsin and chymotrypsin demonstrate that these enzymes may liquefy thick exudates and secretions. Other studies indicate that parenterally administered chymotrypsin hastens the absorption of edema and of blood in the tissues, and that this enzyme acts as an anti-inflammatory agent.[5] Chymotrypsin as a mucolytic agent has been successfully used to reduce peribronchial and intrabronchial edema.[6] The enzyme has been used parenterally in the treatment of chronic otitis, chronic mastoid, chronic maxillary sinus, chronic frontal sinus, chronic ethmoid sinusitis, Eustachian tube synechia, otitis adhesions, diphtheria membrane, croup, and laryngitis edema. Antibiotics were used conjointly with the enzymes.[7]

One group of researchers established the intramuscular use of trypsin as an anti-inflammatory agent,

1. Limber, C. R., et al., *J.A.M.A.*, 149:816-821,1952.
2. Goodard, R. F., & Roorbach, E. H., *J.A.M.A.*, 163:1125-1130,1957.
3. Unger, L., & Unger, A. H., *J.A.M.A.*, 152,12,1953.
4. Reiser, H. G., et al., *Arch. Surg.*, 63:568-575,1951.
5. Jenkins, B. H., *J.M.A. Georgia*, 431-433,1956.
6. Diaz, E. S., Quimar in the Treatment of Asthma, *Sinopsis Medica International.*
7. Muftic, M. K., *Indian J.M. Sc.*, 11:1015-1020,1957.

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TABLE I

RESULTS OF INTRAMUSCULAR CHYMOTRYPSIN TREATMENT

DIAGNOSIS	NUMBER OF CASES	IMPROVED (GOOD TO EXCELLENT)	NOT IMPROVED
Asthma	11	8	3
Bronchitis	20	17	3
Rhinitis	18	13	5
Sinusitis	11	10	1
Totals	60	48	12

but felt that chymotrypsin was to be preferred since it shares the fibrinolytic activity of trypsin without clotting action on the blood. It was also found that chymotrypsin is less toxic by rapid administration than is trypsin.[8] Other studies demonstrated that chymotrypsin has a greater anti-inflammatory action than trypsin.[9] Chemical inflammation, anaphylactoid inflammation, ultraviolet radiation and thermal burns were employed to test the anti-inflammatory activity of both enzymes.

METHODS AND MATERIALS

About 90 per cent of 60 chronic cases were adults in the 17 to 74 year age group. The remainder were children of 3 to 15 years. An aqueous solution of chymotrypsin* representing a proteolytic activity of 5000 units per cc. was used. Children were given 0.25 to 0.5 cc. (1250 to 2500 units), adults were given 0.5 to 1.0 cc. (2500 to 5000 units). All injections were given deep into the muscle, generally the deltoid. Local tissue reactions were rare, as the solution flows freely through a small-gauge needle. Frequency of injections and duration of treatment varied with the severity of the disease. Injections were given once or twice weekly, or more frequently if symptoms were severe.

These patients had previously been helped somewhat with routine allergic management, nose drops and sprays, antibiotics, antihistamines and corticosteroids. Marked improvement resulted when the chymotrypsin was added to the treatment. In some cases, the use of chymotrypsin completely eliminated the need for other medication or treatment.

In the 48 patients who were improved, the raising of mucus was greatly facilitated. Breathing improved, mucus was readily expelled, nasal passages cleared. Some of the asthmatics experienced the satisfaction of normal breathing for the first time in years. Others were able to discontinue the use of nose drops, antihistaminics, antibiotics and the corticosteroids.

REPRESENTATIVE CASE HISTORIES

CASE 1

A white man of 69 had a diagnosis of asthma, emphysema and pulmonary fibrosis. His vital capacity was 28 per cent. Allergic management provided improvement, and his vital capacity was increased to 32 per cent in five days. Chymotrypsin was added to the allergic treatment, and within ten days the vital capacity was increased to 46 per cent. The patient still has some difficulty with stiff, heavy mucus, but is steadily improving.

CASE 2

A white boy of 9 had severe allergic

*Chymar Aqueous,® The Armour Pharmaceutical Company, Kankakee, Illinois.

8. Hendley, C. D., *Arch. Internat. Pharmacodyn.*, 106:164,1956.

9. Miechowski, W. L., & Ercoli, N., *J. Pharmacol. & Exper. Therap.*, 116:43,1956.

asthma of the perennial type. This child suffered with stiff, heavy mucus following an upper respiratory infection. Although antibiotics and expectorants did not help, chymotrypsin cleared the mucus.

Case 3

A white woman of 26 had bronchiectasis with coughing flares during the grass pollen season, plantain pollen season, ragweed season, and on dust and fungus exposure. She was unable to cough up mucus. Repeated bronchial infections necessitated penicillin. Routine allergy management was of some help. After adding chymotrypsin to the treatment, the mucus was easily expelled and penicillin was no longer required.

Case 4

A white woman of 39 had a presenting diagnosis of bronchitis following an upper respiratory infection. Expectorants and antibiotics did not provide relief. Three injections of chymotrypsin cleared the mucus after it had been present for two weeks.

Case 5

A white boy of 9 with allergic rhinitis and bronchitis was well controlled on allergic management. Following an upper respiratory infection, this child had copious, heavy mucus which would not loosen with oral medication. The symptoms cleared rapidly when chymotrypsin was added to the treatment.

Case 6

A white woman of 48 had allergic rhinitis and bronchitis with heavy mucus in the sinuses following an upper respiratory infection. She complained of severe headaches. One injection of chymotrypsin cleared the mucus and stopped the headaches.

Case 7

A white man of 46 had a diagnosis of chronic sinusitis with severe headaches. He was much worse after respiratory infections and did not respond to antibiotics or expectorants. Relief was obtained within eight hours following an injection of chymotrypsin.

Case 8

A white woman of 40 manifested sinusitis following a respiratory infection. One injection of chymotrypsin cleared the sinusitis completely.

DISCUSSION, SUMMARY & CONCLUSIONS

Of 60 patients suffering from chronic asthma, bronchitis, rhinitis and sinusitis who were given intramuscular injections of an aqueous solution of chymotrypsin, 75 per cent showed clinical improvement.

In the majority of these cases, improvement was demonstrated by easier breathing, improved vital capacity, thinning of bronchial secretions, ability to raise sputum more freely and a reduction in the amount of expectoration. X-rays revealed beneficial changes in the bronchial markings. Marked improvement was shown in one to three days in most cases. In some patients the relief was temporary while, in others it was prolonged. In those patients who reverted to their previous condition in a few weeks, second and third courses were found to be as effective as the original course of therapy.

CONTRAINDICATIONS AND SIDE EFFECTS

As chymotrypsin is a protein of animal origin, occasional reactions may occur. In the 60 cases treated, only four reactions were observed. Three of these were of a mild nature and were not considered severe enough to interrupt the course of treatment. The fourth patient developed chills and a large (about 8 inch) indurated area. These side effects can usually be prevented by the use of a small gauge needle, deep intramuscular injection, expelling all of the enzyme before withdrawing the needle, and the concurrent use of suitable antihistaminics.◀

ORIGINAL ARTICLE

Neuromuscular Disorders of the Esophagus

Neuromuscular disorders of the esophagus should be suspected in the patient with dysphagia without a demonstrable organic lesion

FREDERICK S. CROSS, M.D., *Cleveland, Ohio*

Symptoms of dysphagia most frequently lead to the diagnosis of carcinoma, stricture, or achalasia (cardiospasm) of the esophagus. These can be diagnosed by means of barium swallow and esophagoscopic examinations. There is, however, a large group of patients with significant symptoms of dysphagia not presenting this picture. Because of the paucity of objective findings on barium swallow and esophagoscopic examinations, the dysphagia in these patients is an enigma, and such patients may be labeled as psychoneurotic.

Recently cinefluorography and intraluminal pressure studies of the esophagus have been utilized in diagnosis in such cases. These studies enable one to record dynamic changes in the esophagus with movies and pressure tracings in a way superior to the older techniques, which frequently missed or inadequately recorded the important events. By utilizing these new techniques it has been possible to learn more about two basic types of esophageal neuromuscular imbalance which give a clinical picture of esophageal obstruction and dysphagia similar to that found in such organic diseases as carcinoma or stricture of the esophagus.

NEUROMUSCULAR IMBALANCE

Although neuromuscular changes in the esophagus may be seen at all ages, they become more significant

with advancing age. Esophageal neuromuscular imbalance may be primary with no evident etiology, or secondary to a gastric or duodenal ulcer, an obstruction at the esophago-gastric junction, a hiatal hernia, or a central nervous system disorder. Neuromuscular disorders of the esophagus are not necessarily distinct entities but may represent gradations or variations of the same basic condition. They frequently are the cause of many symptoms related to other more obvious changes, such as a hiatal hernia or a diverticulum of the esophagus.

Neuromuscular imbalance of the esophagus may be further subdivided as to whether the problem is one of hypotonicity and hypoactivity, or hypertonicity and hyperactivity. Whatever the basic pattern, both produce the same clinical end result: Symptoms of esophageal obstruction with dysphagia. The term neuromuscular failure has been reserved for the hypotonic, hypoactive esophagus, and the term segmentation for the hypertonic, hyperactive esophagus.

NEUROMUSCULAR FAILURE

Neuromuscular failure as a primary entity occurs more frequently in older, debilitated people. Little can be gained by studying x-rays alone, and esophagoscopy contributes to the diagnosis only in a negative way. Much information can be obtained from careful routine fluoroscopic examination and from cinefluorography. The usual x-ray study reveals that after the contrast material is passed into the upper one-third of the esophagus there is a delay in the passage of the bolus into the distal portion of the esophagus and stomach, especially with the patient in the supine position. With the patient upright, clearing of the esophagus is aided by gravity. Esophageal transit time is usually more than three minutes as compared to about four seconds in the normal. Misswallowing frequently occurs, allowing small amounts of barium to pass into the trachea, and some regurgitation of barium may take place owing to incoordinated activity of the thoracic esophagus. Once the lower esophagus is reached, there is no delay in the passage of the barium mixture into the stomach.

Intraesophageal pressure studies in this condition show hypotonicity and hypoactivity of the entire esophagus. There is virtually complete absence of peristaltic contraction curves in the entire thoracic esophagus. Pressure tracings also show hypoactivity and hypotonicity of the cricopharyngeal muscle, which explains the mechanism of misswallowing and easy regurgitation of esophageal contents into the tracheobronchial tree. As stated previously, patients with neuromuscular failure frequently present the picture of carcinoma of the esophagus with great weight loss, dysphagia, and inanition. No organic obstruction can be demonstrated, however, since the dysphagia has an entirely functional basis.

SEGMENTATION

The term "segmentation" in this report has been called tertiary contractions and spastic pseudodiverticulosis by others. Segmentation is demonstrable with well-timed x-rays, but the dynamics of this disorder can be appreciated only by careful fluoroscopy or cinefluorography. Again, esophagoscopy is helpful only in a negative way. Fluoroscopy and cinefluorography show normal propulsion of the barium into the proximal one-third of the esophagus, but further progress is

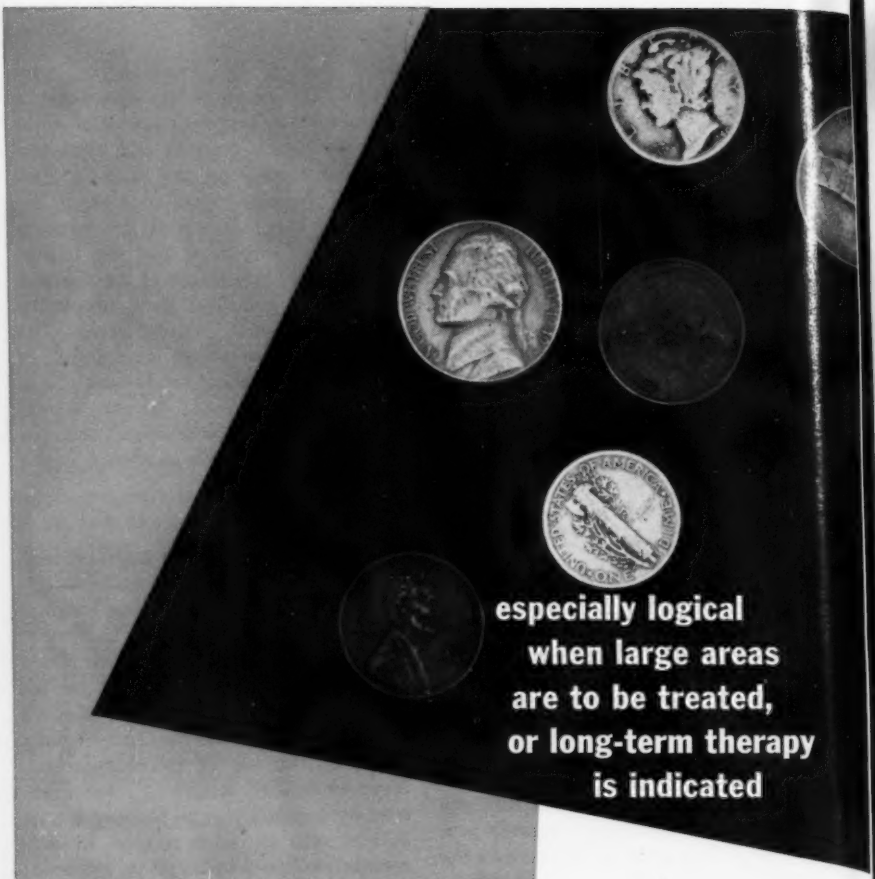
delayed. With barium in the lower one half to two-thirds of the esophagus, segmentation appears as a generalized tone increase with segmental areas of narrowing and pseudodiverticulum formation appearing at the height of the contraction. Incoordinate churning of the barium occurs with considerable retrograde expulsion of barium into the proximal one-third of the esophagus. As the tone increase in the lower esophagus fades, barium is passed from the upper one-third of the esophagus to the lower levels by a second primary wave or by a secondary peristaltic wave. This hyperactivity of the lower two-thirds of the thoracic esophagus prolongs transit time through the esophagus.

Segmentation may be considered a high-pressure problem. This is reflected in the intraesophageal pressure studies which characteristically show the hyperactive and hypertonic state of the lower esophageal segments. Base pressures in all esophageal segments may be high. The peristaltic waves recorded in the upper one-third of the esophagus may be normal, but are more frequently low or absent. The peristaltic waves in the middle and distal thirds of the thoracic esophagus are high and prolonged, with an average pressure three times that found in the normal subject. In effect, the peristaltic activity in the lower two-thirds of the esophagus is exaggerated whereas that in the upper one-third is normal or hypoactive, again indicating the functional obstruction existing between the upper one-third and the lower two-thirds.

Such patients present themselves for study because of severe dysphagia frequently with regurgitation of food during or immediately after meals. The cause of the dysphagia in segmentation becomes apparent when the esophageal movies and intra-esophageal recordings are studied. Passage of the esophageal contents is delayed at the junction of the hypoactive upper one-third and the hyperactive lower two-thirds of the thoracic esophagus, resulting in a functional obstruction with regurgitation. The frequently associated complaint of difficulty in iniating swallowing, or of food sticking in the throat, is explained by hyperactivity of the cricopharyngeus muscle as shown in the pressure studies.

COMMENT

Cinefluorography and intra-esophageal pressure studies are valuable adjuncts in the study of certain esophageal disorders. From such studies it has been possible to learn more about two basic types of esophageal neuromuscular imbalance giving a clinical picture which in the past might have been attributed to psychoneurosis. Neuromuscular failure is characterized by hypoactivity of the esophagus and is seen in older people. In segmentation the esophagus is hyperactive and may be seen at all ages. Neuromuscular failure is the pattern which is found most frequently with hiatal hernia, and in patients with achalasia of the esophagus. Segmentation most frequently is found by itself, but may be associated with other disorders of the upper gastrointestinal tract; *e.g.*, diverticula of the esophagus. Such altered esophageal activity found in association with other disease entities suggests perhaps that the dysphagia of the primary disease may not disappear when the primary disease entity is corrected.◀



especially logical when large areas are to be treated, or long-term therapy is indicated

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ORIGINAL ARTICLE

Treatment of the Common Cold With A New Oral Preparation

A medication combining decongestant, analgesic, antipyretic and antihistaminic actions combats the coryzal syndrome

A. R. STOUGH, M.D., *McAlester, Oklahoma*

More than one drug is usually required to effectively manage the local and systemic manifestations of the coryzal syndrome. This is a report of a series of 707 patients treated with a new tablet* that includes in a single dose four agents known to benefit the diverse symptoms of coryza.[1-9] The medicaments act upon the various manifestations of the syndrome simultaneously in an additive manner.

METHOD OF STUDY

The series was a group of 707 patients suffering from common cold. They were all ambulatory male inmates of a state prison. The age range of the group was 22 to 75 years. They were observed daily during the peri-

**Neo-Synephrine Compound Cold Tablets®*, Winthrop Laboratories, New York, New York. Each tablet contains *Neo-Synephrine* hydrochloride, 5 mg., Acetaminophen, 150 mg., *Thenfadil* hydrochloride, 7.5 mg. and Caffeine, 15 mg.

1. Falk, O. P. J., *Tr. Am. Therap. Soc.*, 30:72,1940.
2. Jackson, C., & Jackson, C. L., Diseases of the Nose, Throat and Ear, W. B. Saunders Co., Philadelphia, 1945, p. 28.
3. Hunnicutt, L. G., *Postgrad. Med.*, 26:625,1956.
4. Morrison, L. F., *A.M.A. Arch. Otolaryng.*, 59:48, 1954.
5. Drill, V. A., Pharmacology in Medicine, McGraw-Hill Book Co., New York, 1954, pp. 21-24.
6. Fox, N., & Livingston, G. S., *A.M.A. Arch. Otolaryng.*, 59:405,1949.
7. Drill, V. A., Pharmacology in Medicine, McGraw-Hill Book Co., New York, 1954, p. 41.
8. Data in the files of the Department of Medical Research, Winthrop Laboratories.
9. Goodman, L. S., & Gilman, A., The Pharmacological Basis of Therapeutics, Ed. 2, The Macmillan Company, New York, 1955, p. 664.

TABLE 1

RESULTS IN 707 PATIENTS TREATED WITH 2 *NEO-SYNEPHRINE COMPOUND COLD TABLETS* DAILY

Number of Patients Treated	Results					
	Excellent		Good		Poor	
	Number	%	Number	%	Number	%
707	196	27.6	363	51.3	148	21.1

od of treatment. Each patient received two tablets three times daily for an average of two to four days, in accordance with their clinical response. The dosage had been previously determined[8] and was found to be suitable for most patients.

RESULTS

Rapid relief from symptoms was obtained in 196 patients, more than one-fourth of the total. A good clinical response was evident in an additional 363, or slightly more than one-half of the group. Adequate relief was demonstrated by nearly four-fifths of the patients. In the remaining fraction, a poor response was reported (Table 1).

A majority of the patients were improved after two days of therapy, and more were relieved in three or four days. Treatment for a longer period was the exception. This appears significant in view of the fact that these individuals were prisoners who might be expected to take advantage of an opportunity to avoid the monotonous daily routine by prolonging any degree of disability.

The patients demonstrated clinical signs such as rhinorrhea, impaired nasal airways, pharyngitis and bronchial irritation with cough, sore throat and sore chest. The usual treatment period was two to four days, with a total of 12 to 24 tablets per patient. A few patients were treated for five or six days, one for 10 days.

NO SIGNIFICANT EFFECT ON BLOOD PRESSURE

Seven normal individuals were given two tablets three times daily for a period of five days to determine effects upon blood pressure. None of the seven showed significant alterations in systolic or diastolic pressure.

SIDE EFFECTS

Although the patients were observed for untoward effects, none were reported.

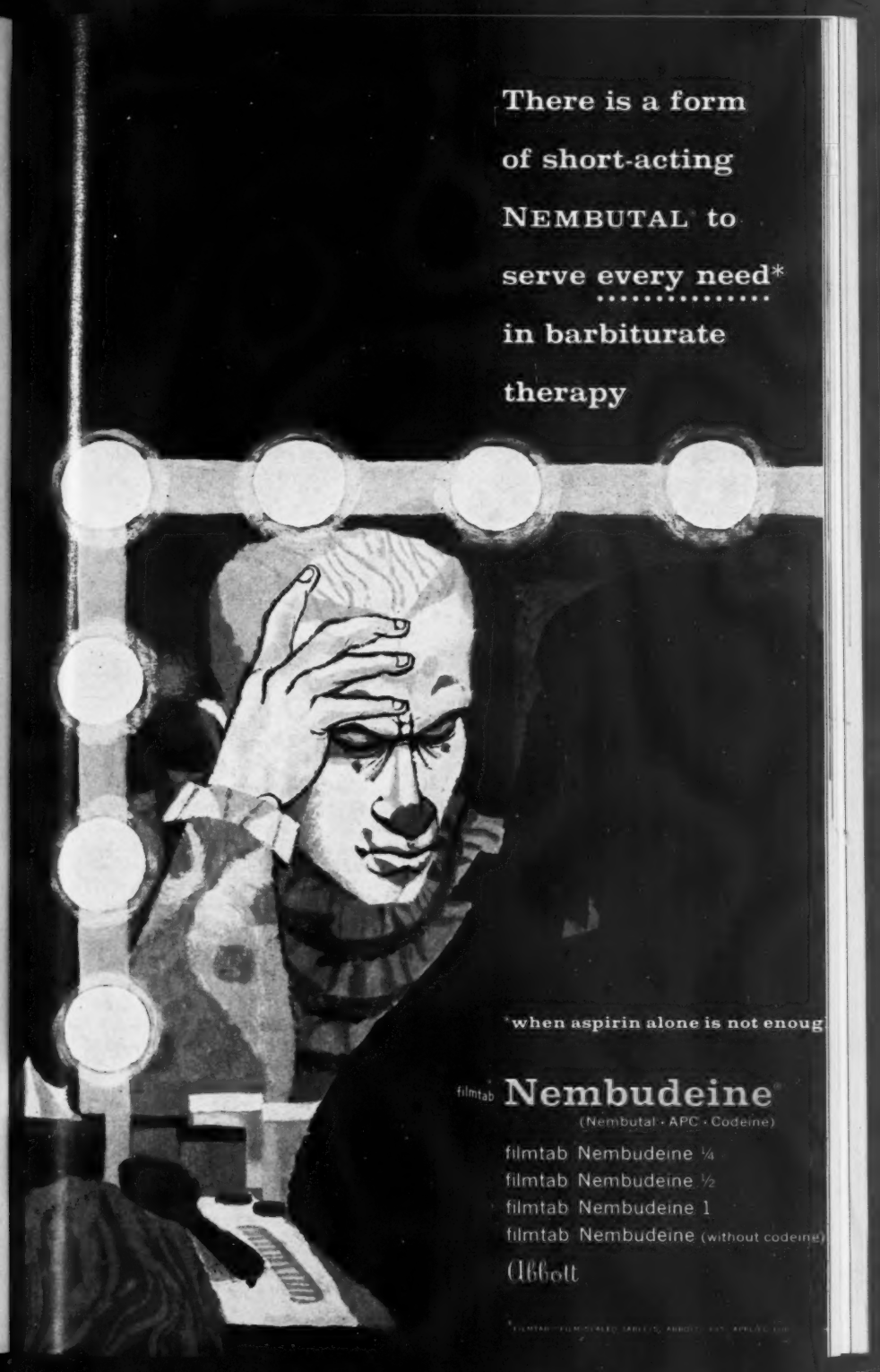
In other studies[8] of more than 500 cases, no major disturbances were attributable to the preparation. Occasionally there was a minor degree of nervousness, drowsiness, dizziness and nausea. The paucity of side effects appears to be valid, inasmuch as it is in line with the findings of others.

Although each tablet contains less *Neo-Synephrine* than will produce an effect on blood pressure,[10] it should be employed with caution in patients with cardiovascular disease or hyperthyroidism, since such persons may be more sensitive to a slight variation in blood pressure or to drugs which potentially affect it.

DISCUSSION

Many combinations of drugs have been offered for the symptomatic treatment of the common cold, many of which have merit. It is difficult to evaluate any one drug or combina-

10. Keys, A., & Violante, A., *J. Clin. Invest.*, 21:1-12, 1942.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filmtab Nembudeine (without codeine)
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tions of drugs in the management of a disease that varies in intensity with each individual, and which presents such a complex mechanism of systemic response to the offending organism. The medication reported here acts upon the symptom complex in an efficient maner. The combination of ingredients attacks the usual symptoms through decongestant, analgesic, antipyretic and antihistaminic action, without significant side effects.

SUMMARY

1. The composition of *Neo-Synephrine Compound Cold Tablets* permits a logical approach to the management of the coryzal syndrome.

2. The convenient dosage schedule—two tablets three times daily—produced good to excellent clinical results in 78.9 per cent of the cases treated.

3. There were no side effects in this series, although occasional minor ones may occur.

4. There was no significant effect upon blood pressure.

5. Results with this preparation indicate that it is a useful drug for the management of the common cold.◀

A Pineal Gland Hormone

The function of the first hormone to be isolated from the pineal gland has not yet been determined. Tests on frogs show that it lightens the skin shade more than any other known substance and reverses the darkening of other hormones.

The quantity of the substance available is small, since more than 250,000 beef glands were required to isolate 1.5 mg. of the new hormone named Melatonin.

Lerner, A. B., et al., *J. Am. Chemical Soc.*, 80:2587, 1958.

ORIGINAL ARTICLE

The Hazard of Postpartum Hemorrhage

Causes of postpartum hemorrhage with recommendations for prevention and treatment are discussed

FREDERICK J. HOFMEISTER, M.D., *Milwaukee, Wisconsin*

Maternal mortality studies reveal that hemorrhage remains the great hazard to the life of the pregnant woman and the new mother. Of 111 maternal deaths studied during a four year period, 61 were due to hemorrhage, an incidence of 55 per cent. In only five instances was the question of hypofibrinogenemia presented as the cause. In six instances failure to promptly diagnose and treat a ruptured ectopic pregnancy resulted in death. However, 31 times ruptured uteri entered into the picture and usually accouchement forcé was the precipitating cause.

CAUSATION

Disturbance of the clotting mechanism, though rare, is a threat under some clearly defined circumstances. The three entities most commonly causative are amniotic fluid embolism, sudden and generally fatal, the rarest; intra-uterine fetal death, more common, must exist for from three to five weeks to be a factor; abruptio placentae with massive retroplacental hemorrhage. Incomplete or slow separation, which permits observation and conservative therapy, is also a factor.

FIBRINOGEN TESTING—A SIMPLE METHOD

Where any of these conditions exist, it is imperative that a routine be established which will include a determination of the fibrinogen content of

the blood. Permitting the blood to clot and then incubating it at 37° C. is a time-consuming procedure. The *Fibrindex Kit** is a rapid and satisfactory method.

We must be aware that disturbance of the clotting mechanism may occur, have a knowledge of how to detect it, and have available in the hospital an adequate supply of fibrinogen for prompt administration in adequate dosages. Fibrinogen can be given two units at a time with further dosage depending on readings after each administration. In some instances as much as 14 units were required to establish levels safe to undertake delivery or other surgical procedure. Fibrinogen can be obtained through the Red Cross Blood Centers and should be kept ready in every maternity unit.

RUPTURE OF THE UTERUS

The 31 cases of ruptured uteri accounted for 30 per cent of all maternal deaths during this four year period. A great danger, therefore, continually threatens in the fourth stage of labor, the immediate postpartum period. The solution points directly toward an awareness of this fact and the prevention of trauma. Most of these deaths are preventable.

MANUAL DILATION A FACTOR

Strangely enough, one frequently encountered cause of trauma is manual dilation. "Manual dilation" has been synonymous with "manual laceration" for the past 25 years. However, instances of its use are still reported and such use is, in some cases, followed by hemorrhage, shock and death. Lifting the impinged edematous anterior lip of the otherwise completely dilated cervix over the head is not to be confused with an attempt to dilate a 2, 4 or 6 cm. cervix to completion by means of "manual dilation." This act borders on assault and should never be attempted.

*Ortho Pharmaceuticals Corp., Raritan, New Jersey.

HIGH FORCEPS

The high-forceps application still enters the picture. This is contemplated destruction and has been outlawed for decades.

CESAREAN SECTION

Primary cesarean section, although often determining the future obstetrical fate of the patient, carries little or no hazard as compared to the high-forceps application. In an 18 year period, 2,348 conservative sections were performed with no maternal deaths. This would not have been the experience with a comparable number of high-forceps applications, or of versions and extractions. One must not misinterpret this statement as advocating the indiscriminate use of section. When indicated it is the most valuable and safest procedure. It should never be denied a woman in order to adhere to some theoretical and outmoded standards of statistics which attempt to indicate the perfect section rate.

VERSION AND EXTRACTION

It would be unjust to state that version and extraction should never be used. However, the indications for its use have been reduced so drastically that it rarely needs to be employed. We are aware of the great hazard of this obstetrical gymnastic procedure, unless all the criteria for its proper use are completely fulfilled: Complete dilation, adequate pelvis, compatible infant and pelvis proportions, deep anesthesia and deliberate and cautious application of maneuver.

Multiparity, especially with the his-

tory of a previous infection, increases the primary hazard of a ruptured uterus. Rupture can also be a real danger when clinicians feel that the second of twins must be delivered by version and extraction. The danger to the infant as the result of version cannot be dismissed. Neonatal surveys indicate that this equals or exceeds the danger to the mother. In the case of a second twin presenting, it is safer to rupture the membranes, guide the head into the canal and deliver with forceps.

PITUITARY RESURGENCE

The use of pituitary derivatives has suddenly bounded back into popularity. Always accepted as a hazard, single-shot doses have been replaced by intravenous drip *Pitocin.** Many physicians advocate repeated infusions as a method of ripening the cervix. On well supervised services, under constantly watchful eyes, the hazard may not be great. However, spontaneous rupture of the uterus with apparently spontaneous dilation of the cervix to completion and precipitous delivery have been reported, also associated with subsequent hemorrhage, shock and death. Multiparity again increases the hazard. It is questionable whether pituitary derivatives should ever be given the grand multiparous patient. The hazard of previous intrauterine infection with resultant low-segment damage makes stimulation especially dangerous to such a patient. The danger of individual patient response and sensitivity can not be foreseen. Amniotomy and patience are suggested when all the criteria essential to induction are present. The criteria that should always exist are: Presenting part (head) engaged, cervix "ripe" and cervix dilated and dilatable. Without these fulfilled and without the existence of necessity for emergency delivery, abdominal delivery is suggested as the safer choice.

*Parke, Davis & Company, Detroit, Michigan.

USE OF OTHER FORCEPS

Mid-pelvic application of forceps in the case of arrested labor, or the routine use of the outlet forceps, introduces an additional factor of trauma to both cervix and vagina. The use of wide episiotomies, mediolateral, or mid-line before attempted rotations, knowledge that dilation is *complete,* and an exact knowledge of the position before attempted rotation, are essential steps in preventing trauma. An additional safety factor would be an attempt at manual rotation.

EXTRA CAUTION IN CASES OF PREVIOUS SECTION

Prevention of traumatic hemorrhage can be effected by caution in handling the previously sectioned patient. A large percentage of these patients can subsequently be delivered from below, although certainly never where disproportion is a factor, questionably when the previous section was a classical one, and not if more than one previous section has been done. It is essential, in case of previous section, that the attending physician be familiar with the type of section done, whether subsequent section or vaginal delivery is anticipated. All should be aware of the fact that chance of spontaneous rupture of the uterus is doubled by previous classical section. Multiparity increases the hazard of rupture of a section scar. A history of infection is also a danger signal and history of a prolonged labor before section is a warning. A sudden violent labor in a patient previously sectioned should be regarded with suspicion. If this haz-

ardous ordeal is undertaken, it is the duty of the attending physician to remain in the hospital in constant attendance until delivery is successfully effected.

NO ENTIRELY SAFE METHOD

Not all the danger is erased when the decision is made to follow a previous section with a second or third elective section. Maternal death has resulted from spontaneous uterine rupture secondary to very early and mild labor occurring during the night preceding the date of the scheduled repeat section. The nurses on the obstetrical floor must be fully indoctrinated with the necessity of requesting the patient to report any unusual sensations or contractions. This report must be relayed to the attending physician who then has the responsibility of responding *immediately*. Furthermore, the surgical service should be alerted and surgical set-up made immediately, even though it may prove a false alarm. For emphasis it must be stated that in the State of Wisconsin, during one 12 month period, 22 instances of hemorrhage resulted in maternal deaths. These 22 deaths included 15 ruptured uteri!

THE THIRD AND FOURTH STAGES

Hemorrhage during the third and fourth stages of labor are responsible for many more of the maternal deaths. Blood and blood expanders must always be available in every hospital that assumes the responsibility of the care of maternity cases. The immediate postpartum patient should be returned to a recovery room, to remain until responding and until there are no signs of hemorrhage. The use of the obstetrical recovery room must be universally accepted.

The placenta should be delivered as soon as possible after the delivery of the infant, and before the episiotomy is repaired. It is our belief that the placenta separates during the delivery in the majority of instances. When it does not immediately follow delivery by the usual methods, it is trapped by the cervix. We then aggressively manually remove it, although this is not without hazard. The uterine cavity must always be carefully palpated after this procedure and uterine perforations must be discovered or ruled out. Every obstetrical set-up should have two Jackson retractors and three ring forceps. These instruments permit the next step, inspection of the vault and visualization and inspection of the cervix. In case adequate assistance cannot be obtained, the Gelpi retractor will afford sufficient exposure of the cervix and vagina. Lacerations can be associated, and unsuspected, in spontaneous delivery. At Milwaukee Hospital in one half of the cases, postpartum blood loss occurred with spontaneous labor. Routine inspection will rule out or reveal lacerations of the vault or cervix, and any unsuspected inversion of the uterus.

INTRA-UTERINE EXAMINATION

In 3,260 consecutive deliveries I have routinely done intra-uterine palpation to rule out or reveal the existence of intra-uterine lacerations and retained tissue. This has been done as a teaching maneuver and without ill result. When bleeding continues without evidence of vaginal or cervical laceration, intra-uterine palpation is safe and necessary. Following the routine of delivery, infant and placenta inspection, palpation and repair of episiotomy eliminate all causes of hemorrhage except one. According to our survey, atony led in the list of


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*Biegeleisen, H. L.: Clinical Medicine; Oct., 1955
*Roberts, J. T.: Clinical Medicine; Nov., 1957

causes in the immediate postpartum period. The use of large doses of intravenous drip *Pitocin*, with intrauterine palpation and bimanual pressure will effectively control this complication. Constant observation, preferably in the obstetrical recovery room, is essential.

PROMPT REPAIR

Any lacerations of vagina or cervix however small are to be immediately and accurately repaired, to reduce future erosions, eversions, chronic cervicitis and possibly even cancer to a minimum. Lacerations extending into the body of the uterus and often into the broad ligament may require repair of the vaginal lacerations and total abdominal hysterectomy. Adequate blood replacement, under pressure and through several veins, may be required before, during and after surgery. The great breach of therapy has been doing an abdominal subtotal hysterectomy, permitting the bleeding cervical and vaginal laceration to continue pouring out blood, sometimes resulting in shock and death.

SUBSEQUENT PREGNANCY

Rarely, depending upon the obstetrical experience of the patient and the extent of the tear, the laceration can be repaired and subsequent pregnancy permitted. Caution must be exercised during the prenatal observation of such a patient and delivery should be by the abdominal route.

SUMMARY

An attempt has been made to reveal the personal experiences of a member of a maternal mortality committee, and to correlate these with experiences in a private obstetrical practice. Hemorrhage is the leading and constant threat. Trauma must be avoided. Intelligent, thorough examination, administration of sufficient blood for replacement, and immediate and adequate corrective surgical therapy are earnestly urged. Obstetrics is major surgery and must be approached and carried through as such. Adequate equipment and facilities to cope with surgical problems must be a part of any obstetrical unit; this includes equipment and personnel to administer anesthetic agents, a sufficient supply of blood or blood expanders, a thoroughly obstetrical recovery room and personnel to staff it.

Where these requirements are met, the so-called irreducible maternal mortality rates will be further reduced.◀

ORIGINAL ARTICLE

Occipito-Cervical Pain, Referred Pain, Headache Prolotherapy

Excessive ligament-tendon relaxation causes transmission of afferent sensory nerve impulses to the brain where they are interpreted as pain

G. S. HACKETT, M.D.,* *Canton, Ohio*

The most frequent cause of *chronic* occipital and cervical disability is incompetence of the ligaments and tendons to maintain stabilization and permit motion without pain, such as frequently persists following "whiplash" injury.

PATHOLOGY

Sprains and tearing of the ligament and tendon fibers take place chiefly at their bony attachments. Normal repair, in response to sensory stimulation, occurs with the proliferation of new cells to re-establish a strong attachment to bone.

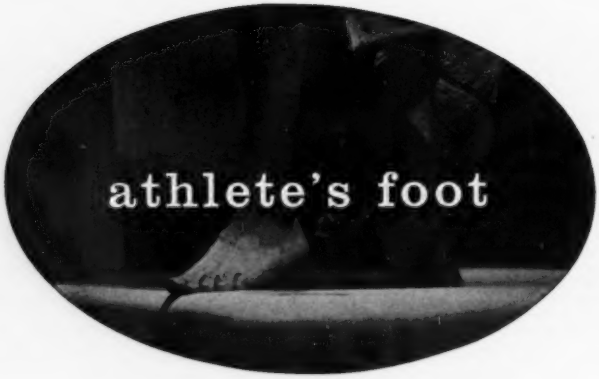
This proliferation usually strengthens the fibro-osseous attachment in a few weeks, but in more severe cases a firm attachment may not take place, so that a weakness remains and normal tension will stretch the weak ligament/tendon fibers. This weakness or instability is known as *ligament/tendon relaxation.*

There is an abundant supply of sensory nerves within the ligaments and tendons near their bony attachments.[1,2] Traction on nerves causes pain.[3]

When a strong attachment of liga-

*Consulting Surgeon, Mercy Hospital.

1. Leriche, R., *Gaz. d. hop.*, 103:1294,1930.
2. Gardner, E., *Stanford M. Bull.*, 11:203,1953.
3. Lennander, K. G., *Zentrabl. Chir.*, 28:209-223, 1901.



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ment (includes tendons throughout this manuscript) to bone does not take place following injury, the fibers stretch under normal tension and permit an abnormal tension-stimulation of the non-stretchable sensory nerve fibrils, causing a bombardment of sensory impulses which are transmitted to the cerebrum, where they are interpreted as pain.[4]

Tendon relaxation occurs at the attachments of the cervical muscles to the occipital bone beneath the curved occipital line, and to the spines, lamina and transverse processes of the cervical vertebrae. Ligament relaxation of the cervical vertebrae occurs chiefly in the interspinus and articular ligaments.

SYMPTOMS

The chief symptom of ligament/tendon disability is pain. There is local trigger-point pain at the attachment to bone. When the bombardment of somatic-sensory impulses from the relaxed ligament enters the posterior horn cells, there is frequently a stimulation of other afferent impulses that enter the same cell. This is transmitted to the brain where it is interpreted as pain from another part of the body (referred pain).

Headache is a common form of referred pain of somatic origin from occipital tendon relaxation, and to a lesser extent from the attachments of the relaxed ligaments and tendons to the cervical vertebrae.

The referred pain from the occipital tendons extends up over the scalp to the forehead on the same side and back of the eye, so that the patient sometimes cannot read or endure light.

There is sometimes a loss of equilibrium associated with headache, particularly when arising from a stooped position.

Relaxation of the cervical interspinus ligament is essential to joint instability or any abnormal movement of one vertebra on another, and to relaxation of the cervical articular ligaments on one or both sides. There is local pain and trigger-point tenderness of the interspinus ligament, but no referred pain beyond two to three inches from the midline.

Somatic referred pain to any extent away from the spine has its origin in the articular ligaments. From the articular ligaments in the upper cervical area, the referred pain extends laterally to the neck. From the mid-cervical area, the pain is referred above the shoulder, the anterior arm and forearm, and to the thumb, first and second fingers. From the lower cervical area, the referred pain is below the acromial process of the scapula, and down the antero-lateral surface of the arm and forearm.

Somatic referred pains jump the large joints of the upper extremity as they do the lower extremity.

Patients with a high pain threshold rarely have referred pains, and their ligament relaxation is greater before they are conscious of local pain. Consequently, they require more treatment to accomplish joint stabilization than their symptoms would indicate.

DIAGNOSIS

The diagnosis of ligament/tendon relaxation is by trigger-point tenderness on pressure with the thumb at the fibro-osseous junction. It is readily obtainable in the occipito-cervical area when the patient is comfortably seated astride a chair with his arms resting on the back of the chair. The examiner's left hand steadies the head

4. Brain, W. R., Diseases of the Nervous System. London, Oxford Univ. Press, 1951.

to relax the muscles while the right thumb elicits trigger-point tenderness in the area designated by the patient.

The diagnosis is confirmed by intraligamentous needling with a local anesthetic solution. The irritation of the needle and the pressure of the anesthetic solution immediately reproduces the local pain with intensity. This disappears within two minutes as anesthesia takes place. The patient is convinced, his confidence is won, and he is anxious to proceed with the treatment.

TREATMENT

The treatment of ligament/tendon relaxation is by prolotherapy (the rehabilitation of an incompetent structure by the proliferation of new cells). The technic consists of the intraligamentous injection of a proliferating solution combined with a local anesthetic to stimulate the proliferation of new bone and fibrous tissue cells to strengthen the "weld" of fibrous tissue to bone. It permanently eliminates the pain and stabilizes the joint.

The injections consist of less than 0.5 cc. of the solution distributed at each of several contacts with bone, to avoid pooling of the solution and accomplish a larger area of cell proliferation.

The treatments are given with the patient prone, with two pillows under his chest, so that his forehead rests on the table to eliminate the lordotic curve of the cervical spine.

The treatments are given in the office, except to a small percentage of patients with extreme disability. The treatments are not given in the acute stages, but two or three months afterward if the disability continues. Several treatments can be given at one time.

The proliferation of new cells becoming permanent continues for approximately six weeks. The patient returns for re-examination two months after the last treatment.

The proliferant that has been used for 19 years is *Sylnasol,** one part combined with three parts of *Pontocaine,* 0.15%.† A zinc sulfate solution has also been used extensively.

(Details of diagnosis, proliferants, technic of treatment, and medication are fully presented in the third edition of the author's book on ligaments.[5])

ANIMAL EXPERIMENTS

Animal experiments on fibro-osseous proliferation in rabbits were reported in 1955.[6] X-rays revealed a large increase of both bone and fibrous tissue at the fibro-osseous junction.

Microphotographs of demineralized specimens revealed the proliferated intergrowth of new bone and fibrous tissue strands which strengthen the "weld" of fibrous tissue to bone, which accounts for the amazing results that have been obtained clinically in strengthening ligaments, stabilizing articulations, and permanently freeing patients from painful somatic disability.

STATISTICS

During the past 19 years, 1689 patients with ligament/tendon relaxation have been treated.

Approximately 18,000 intraligamentous injections have been made. There were no unfavorable sequelae and 82 per cent consider themselves permanently cured. Age range was from 15 to 85 years, duration of disability from 3 months to 65 years,

*G. D. Searle & Co.
†Winthrop Laboratories

5. Hackett, G. S., Ligament and Tendon Relaxation. Third Edition. Chas. C. Thomas Co., Springfield, Illinois, 1958.
6. Hackett, G. S., *Arch. Surg.*, 73:78,1956.

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Pyridoxine (B_6)	1 mg.	Fluorine (CaF_2)	0.015 mg.
Niacinamide	10 mg.	Copper (CuO)	0.15 mg.
Riboflavin (B_2)	2 mg.	Iodine (KI)	0.01 mg.
Vitamin B_{12} with AUTRINIC Intrinsic Factor Concentrate	1/6 U.S.P. Oral Unit	Potassium (K_2SO_4)	0.835 mg.
		Manganese (MnO_2)	0.05 mg.
		Magnesium (MgO)	0.15 mg.
Ascorbic Acid (C)	50 mg.	Molybdenum ($Na_2MoO_4 \cdot 2H_2O$)	0.025 mg.
Vitamin K (Menadione)	0.5 mg.	Zinc (ZnO)	0.085 mg.
		Calcium Carbonate	575 mg.

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with an average of 4½ years. Some who were successfully treated had previously submitted to as many as six spine operations, including laminectomy, fusion, and cordotomy. Others were treated by traction, manipulation, braces, and injections of alcohol, cortisone and local anesthetics.

Some had undergone psychiatric treatment, including shock. Others had become addicted to narcotics. Many had been told they had ruptured, slipped, or crushed discs, and had been advised to learn to live with their disability and return for an operation if the condition got worse. Others were advised by eminent surgeons not to submit to any operation.

OBSERVATIONS

Painful ligament/tendon relaxation occurs chiefly in the congenitally loose-jointed individual who has a limited capacity for fibro-osteogenesis. Their x-ray reports are usually negative.

The close-jointed individual, possessing adequate capacity for fibro-osteogenesis, develops a substantial fibro-osseous junction of ligaments to bone. When sprains do occur, the repair by fibro-osseous proliferation is usually sufficient to provide tensile strength, so that ligament relaxation seldom results. However, in response to somatic sensory stimulation, the close-jointed individual is prone to develop painless periarticular and osteoarthritis by fibro-osseous proliferation at the ligament/tendon attachment. Sometimes complete bridging of the joint occurs, without much discomfort.[7,8]

To determine if a patient is loose-jointed, the fingers, elbow and knee can be well extended beyond a straight line, and the thumb extended to approach the radius, while the wrist is in the position of flexion.

SUMMARY

There is more chronic occipital and cervical pain, and referred pain to as far as the eyes and fingers, from ligament/tendon relaxation (incompetent to maintain normal tensile strength), than from any other entity.

The fibers of relaxed ligaments stretch under normal tension and permit an abnormal stimulation of the non-stretchable sensory nerves within the ligament. Afferent sensory nerve impulses are transmitted to the brain, where they are interpreted as pain.

The diagnosis is confirmed by intraligamentous needling with an anesthetic solution.

Disabled ligaments/tendons are permanently strengthened by prolotherapy (rehabilitation of an incompetent structure by the proliferation of new cells). It is the method of choice for joint stabilization.◀

7. Hackett, G. S., *J.A.M.A.*, 163:183,1957.
8. Hackett, G. S., & Henderson, D. G., *Am. J. Surg.*, 89:968-973,1955.

ORIGINAL ARTICLE

Factors in the Early Detection of Diabetes Mellitus

Some methods used to screen diabetics including urine sugar, fasting blood sugar and glucose tolerance tests, are reviewed

ALBERT F. TETREAULT, M.D., *Providence, Rhode Island*

Today there are many potent agents to facilitate carbohydrate metabolism. By their early and effective use diabetics suffer fewer vascular complications, experience a greater resistance against infection, and enjoy a longer life. The subclinical diabetic can also share in these benefits if he is made aware of his disease and instructed in its management.

DIAGNOSIS

The time-honored urine sugar tests faithfully confirm glycosuria in known or severe diabetes, but fail in the detection of mild or potential diabetics. This is also true of a single, fasting blood sugar (F.B.S.). Recently, 80.3 per cent of a group of 997 subjects[1] had borderline or abnormal glucose tolerance tests, but normal fasting blood sugars.

The ideal screening method would place all subjects under carbohydrate stress and be of sufficient sensitivity to discover all cases of potential diabetes. The procedures that have been proposed differ according to the quantity, quality, or mode of administering a test meal, as well as the frequency of blood sampling. The one dose, two-hour glucose tolerance

1. Petrie, L. H., et al., *Ann. Int. Med.*, 40:963-967, 1954.

test has been proposed.[2] Taking random blood sugars 2½ to 3 hours after 100 gm. of glucose has been suggested.[3] Examination of a single blood sample taken two hours after the intravenous injection of 25 gm. of glucose has been proposed on the basis that a patient with glycosuria had a 10: 1 chance of not being diabetic if the blood sugar fell to normal within two hours.[4] After comparing four diagnostic glucose tolerance tests, the significance of the two-hour postprandial blood sugar test was confirmed and a standard meal, considered an excellent presumptive test although more gross and variable than those employing glucose, was suggested.[5] Exclusive of pathological hypoglycemia[6] the two-hour, postprandial blood sugar value is generally considered to be one of the most satisfactory means of differentiating between normal and abnormal glucose tolerance.

A SERIAL STUDY

Recently, 1114 consecutive admissions to a general hospital were studied[7] with particular reference to primary admitting diagnoses, age, nationality, and some of the factors said to affect carbohydrate metabolism. Of the five screening tests performed, the smallest percentage, (27%) of the cases with decreased glucose tolerance was found when only a urine sugar test was performed. The percentage rose to 33% when both a urine sugar test and a F.B.S. were done on every patient. Over 50 per cent of the cases had some form of glucose intolerance when a two-hour postprandial test was part of the screening procedure. This study also revealed that the latter test was not only more sensitive and reliable than an F.B.S., but if taken two hours after an average breakfast was also adequate for uncovering potential diabetics.

PITFALLS IN DIAGNOSIS

For an alimentary tolerance test a preparatory diet must be given, and severe dehydration, starvation, bowel obstruction, severe diarrhea, gastrectasia, extensive atrophy or ulceration of the gastrointestinal mucosa, adhesions preventing normal peristalsis must be ruled out. Hyperglycemia and/or glycosuria may be influenced by a high fat diet, hyperpituitarism, hyperadrenalism, Paget's disease, toxemia, prolonged bed rest, gastrectomy, jejunectomy and acromegaly. One abnormal test or one abnormal glucose tolerance curve, should not serve as a basis for a positive diagnosis.[8] Most of the factors adversely affecting glucose tolerance can be avoided in ambulatory patients. In the hospital, ability to handle carbohydrate depends upon:

1. The severity of illness: The stress of an illness or an operation may cause an outpouring of epinephrine which depletes the stores of glycogen in the liver and impedes the combustion of carbohydrate by the peripheral tissues. This inhibitory action may be enhanced by the glucocorticosteroids and reflected as transient, benign hyperglycemia and/or glycosuria.

2. The state of nutrition and hydration: The longer they fast, the greater carbohydrate metabolism will be affected. A fast of only 40 hours ma-

2. Mosenthal, M. O., & Barry, E., *Ann. Int. Med.*, 33:1175-1194,1950.
3. McCullagh, E. P., & Zwickel, R. E., *J.A.M.A.*, 52:1031-1035,1953.
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8. Spellberg, M. A., & Leff, W. A., *J.A.M.A.*, 129: 246-250,1945.

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terially reduced carbohydrate in man. Alimentary sugar curves were prolonged and glycosuria appeared.[9] An increase of ketonuria within a few hours of the omission of a meal has been demonstrated.[10]

3. Age: Glycogen stores in the body are more readily exhausted in the young than in the older patient; the younger the child the sooner hypoglycemia[11] and ketosis appear following a fast.[12] In the 20 year old group, heredity and obesity are of little importance as causes of diabetes.[13] Investigation of glycosuria occurring under the age of 20 showed that only 30 per cent of the patients were diabetic.[14] The highest incidence of abnormal carbohydrate metabolism has been ascribed to those over 70.[1]

4. Sex, race, and nationality: The incidence is the same in the two sexes. Negro females are more prone[1] than negro males. There was a significant predilection among the Jewish and Irish.[15] Among those long in this country, the incidence of diabetes was much less. Glycosuria was highest in the Canadian-French.[16]

5. Weight: Most obese adult patients utilize ingested glucose slowly.[12] The altered carbohydrate tolerance in obese women without glycosuria appears to be related more to the duration (more than 11 years) than to the degree of obesity.[17,18] Other evidence indicates that the fatty tissues of obese diabetics have a reduced capacity for taking up glucose.[19] But are obese patients with glucose intolerance truly diabetic? It has been demonstrated that if glycemia and glycosuria are seen following the ingestion of 100 gm. of glucose, early diabetes is probably the explanation.[20]

9. Peters, J. P. & VanSlyke, D. D., Quantitative Clinical Chemistry. Interpretations. Second Edition, Vol. 1, Williams and Wilkins, Baltimore, 1946. p. 147.
10. Ibid, p. 489.
11. Talbot, F. B., et al., *J.A.M.A.*, 83:91:93,1924.
12. Peters, J. P. & Van Slyke, D. D., Quantitative Clinical Chemistry. Interpretations. Second Edition. Vol. 1, Williams and Wilkins, Baltimore, 1946. p. 486.
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16. Blotner, H., *J.A.M.A.*, 131:1109-1114,1946; correction 131:1449,1946.
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19. Tornblom, N., & Hellman, S., *J.A.M.A.*, 154: 1459,1954.
20. Beeler, C., & Fitz, R., *Arch. Int. Med.*, 28: 804-812,1921.

SUMMARY

A comparison of the procedures used to screen diabetics reveals that a blood sugar drawn two hours after the ingestion of an average breakfast is adequate for the detection of potential diabetics.◀

Urinary Excretion of Radioactive Vitamin B_{12} in Carriers of *Diphyllobothrium Latum*

Seven anemic and 50 nonanemic patients harboring *Diphyllobothrium latum*, the fish tapeworm, 16 patients with genuine pernicious anemia, and 50 healthy controls were subjected to Schilling's urinary radioactivity test. Anemic and nonanemic worm carriers excreted significantly lower amounts of radioactive vitamin B_{12} in the urine than did the normal subjects, the anemic subjects exhibiting the lowest values. The urinary excretion increased significantly after the expulsion of the worm. This supports the earlier view that, even in nonanemic carriers, *D. latum* impairs vitamin B_{12} absorption and is thus able to take up the vitamin in spite of the presence of intrinsic factor. The possibility is pointed out that the worm named *D. latum* is not the same species in different parts of the world.

Nyberg, W., et al., *New England J. Med.*, 259:216-219,1958.

How Should We Treat Rheumatoid Arthritis?

Rest, passive exercises, and judicious use of medications contribute to the comfort of the patient

RUSSELL L. CECIL, M.D., *New York, New York*

Of the fundamentals of the treatment in rheumatoid arthritis, rest is the great starting point, the amount and degree depending on the severity of the attack and the circumstances involved in the instant case. The emotional state has much to do with the course of the disease. Unfortunately it is often easier to discover the patient's fear or resentment than it is to banish it.

Along with rest and his own psychotherapy, the doctor will probably institute physical therapy—in a hospital bed, in the office or in the clinic.

Daily exercises in a warm pool are agreeable to the patient and beneficial in building muscles and morale. The patient sleeps better and his appetite improves. Most important is the effect of the exercises on the swollen, painful joints. On this routine of bed rest and exercises in the pool, nearly every rheumatoid patient will show an improvement, which is rapid in some cases. A warm pool is not always available. Most departments of physiotherapy have a Hubbard tank or two, which is almost as good as the pool. If the patient is not too crippled, the pool exercises (often passive) should be supplemented by daily active bed exercises for arms, back and legs. Flat on his back, a systematic group of calisthenics is rehearsed with him by the physician or physiotherapist.

These first few weeks or months of treatment represent a crucial period of reassurance and re-education. A reasonable degree of comfort can nearly always be achieved by generous doses of aspirin, supplemented if necessary by codeine or demerol. Local heat is part of this routine for comfort. There is no reason why meprobamate or chlorpromazine should not be useful in some of the emotionally disturbed.

Gold salts are the oldest of the drug treatments that may alter the course of the disease. Salicylates antedate gold salts, but have little more than an analgesic effect. About 60% of cases treated with gold salts have a remission or show improvement. In a 20-year follow-up study, 75% relapsed sooner or later, but the remissions sometimes lasted a number of years. Best results are obtained in early and active cases.

In the early days of gold therapy, serious and occasionally fatal complications were encountered. Today one rarely gives more than 50 mg. of the gold salt intramuscularly once a week. On this dosage we have rarely encountered a sharp reaction. When gold rashes occur, the treatment should be stopped for a week or two and BAL or corticosteroids administered. The gold treatment can be resumed at a smaller dosage as soon as the rash has faded. The most popular gold salts in this country are the soluble salts.

Administration of any of the steroids suppresses the inflammatory process in nearly all of the rheumatic diseases, including rheumatoid arthritis. The disease is not checked however, and when steroid therapy is discontinued the arthritic swelling and pain promptly return, sometimes in aggravated form. The steroid "remission" is not a true remission, nor is this rebound reaction after cessation of cortisone therapy a true relapse.

Prednisone and prednisolone are three or four times stronger than hydrocortisone, cause little or no retention of sodium and water, and the therapeutic effect is even more striking than that of cortisone or hydrocortisone. However, peptic ulcer and osteoporosis (with or without compression fracture) seem to occur more frequently with prednisone and prednisolone than with cortisone and hydrocortisone.

The larger the dose and the longer the course of steroid therapy the greater the chance of dangerous side effects. It is well to try to work the daily dose of prednisone down to 10 or 15 mg. a day. Salicylates may be used to supplement the steroid treatment. Every patient should have a vacation from steroid therapy at least once a year, and sometimes the vacation can be a permanent one. Cortisone is not routine therapy in rheumatoid arthritis. It may be used in the beginning of severe cases to tide over the rough period, or perhaps after more conservative measures have failed. The average case can be well handled without recourse to steroids.

Positive contraindications to steroid therapy are peptic ulcer, osteoporosis, diabetes mellitus, tuberculosis, other active infections, psychoses or severe psychoneuroses. The incidence of peptic ulcer as a side effect of cortisone therapy ranged from six to 34%. The larger the daily dose of steroid, the higher the incidence of ulcer. Many physicians give antacids or cholinergic drugs along with steroid therapy, but there are no figures on efficacy at present.

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is seen with osteoporosis even on conservative treatment. "Postmenopausal" osteoporosis is also common, but that produced by long-sustained steroid therapy (either in arthritis or in other conditions) is severe and apparently analogous to the osteoporosis of Cushing's syndrome.

In a series of 15 patients with rheumatoid arthritis who had received prednisone for one to two years, fractures were encountered in five (33%), a distressingly high proportion of cases. The effectiveness of the sex steroids and of dietary calcium in protecting the bones during cortisone therapy has not been established.◀

Mississippi Valley M.J., 80:165-168,1958.

Etiologic Factors in Acne Vulgaris

The prevailing view of acne vulgaris is that the acne of adolescence results from a sebaceous gland dysfunction in which there is an androgen and progesterone/estrogen imbalance, the androgen predominating. The androgens and estrogens first elaborated at adolescence are produced throughout most of mature life when acne vulgaris is not common.

The sebaceous glands enlarge during adolescence, and the secretion of sebum is proportionate to the gland surface. The sebum output falls to a stationary level between the ages of 20 and 25, while the gland surface area remains the same.

In acne, the hair follicle adjacent to the sebaceous gland is filled with a hyperkeratotic or parakeratotic plug. One factor which may precipitate acne in the beard area is the absence of an effective hair through the follicle opening. The wall of the hair follicle adjoining the sebaceous gland contains a stratum granulosum during early acne. The follicle plug in acne is the result of altered protein metabolism.

The sebaceous glands, the site of acne, have no demonstrable innervation but are acted on by endocrine secretions. Since acne occurs in both sexes, it cannot be related solely to gonadal hormones. Administration of the androgenic steroid, testosterone, can produce an acneiform eruption, yet, even in males, 50 to 70 per cent of body androgenic steroid derives from the adrenal cortex. Frequently, there is premenstrual aggravation of acne vulgaris simultaneous with decrease in progesterone. The pituitary growth hormone acts directly on body structures, not by means of an endocrine gland.

Acne may be more severe in the tropics where sweating is pronounced. Sebum spreads much more rapidly on a wet skin than on a dry one. From the data thus far, it appears that the anterior pituitary gland, the adrenal cortex, and eccrine sweating all play roles in the disturbance called acne. All of these areas are under direct or indirect control of the hypothalamic portion of the brain. Perhaps the emotional problems of puberty starts the entire series of events which bring about the comedo of clinical acne. At present, only a suspicion can be recorded that it is related to unusually severe problems of adaptation. The role of heredity and ancestry is moot.

Warshaw, T. G., *New York J. Med.*, 58:2960-2962, 1958.

Treatment of the Burn Wound

Clotted plasma exudate forms an eschar which may be more protective in burn cases than medication

CARLYLE E. WILSON, M.D., and
SAMUEL A. SWENSON, JR., M.D., *Omaha, Nebraska*

The quickest and most certain method of "closing" a burn wound is to allow the surface plasma-exudate to clot. The plasma-crust (eschar) is a biological cover second in value only to skin, and is a sufficient dressing until healing is completed. Organisms found on or in the crust do no harm. Do nothing to delay the formation of the eschar, or to disturb its integrity, unless infection or cracking develops. Local medicaments—antiseptic solutions, tanning solutions, ointments—have only contributed further irritation to raw surfaces, or kept them moist and soggy, providing a favorable medium for growth of microorganisms.

WHAT GOES ON UNDERNEATH

The exudate of a partial-thickness burn dries in 48 to 72 hours. Epithelial regeneration proceeds beneath the crust and is usually complete in 14 to 21 days. In the deeper second-degree burns 21 days are required. In a third-degree, or full-thickness burn, there is dehydration of the pearly white, or charred dead skin. This is converted to a protective eschar in the same period of time as in partial-thickness burns. Liquefaction occurs in 14 to 21 days beneath this eschar. If there is doubt as to the depth of the burn, periodic observation of the eschar is often helpful. In second-degree burns, either superficial or deep, the eschar

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will begin to curl as soon as re-epithelization takes place beneath. In third-degree burns the eschar remains level with, or below, surrounding skin.

TRANSPORTING THE BURN PATIENT

For transportation to the hospital, cover with a clean sheet, and give 1/6 grain of morphine intravenously. If more than a half-hour trip, a larger dose plus a plasma-volume expander may be required. After 24 hours patients do not tolerate transportation well. Upon admission, the patient is taken directly to a room where all personnel, including the patient, are capped and masked. All of the patient's remaining clothing is removed, and the burn wound thoroughly inspected under good light. All loose epithelium is sharply debrided. Cleansing with sterile cotton balls soaked in warm solution usually suffices (grease or oil may require a detergent solution), then thoroughly rinsing or irrigating with warm sterile saline is done.

COMPLETE EXPOSURE PREFERRED

Most patients prefer to remain completely exposed. A clean sheet is draped over the patient and supported by a overhead rod running down the middle of the bed. It is best to keep the patient in a private room at normal hospital temperature, until the eschar has formed.

If the burn is circumferential involving the trunk, it is preferable to employ the closed method or a Stryker frame, turning the patient every two or three hours. The patient may be placed on his back or abdomen, lying on vaseline gauze, with heavy absorbent gauze over the bed.

ATTENTION TO CRUST

The crust that forms during exposure may be heaped up by escaping serum. These should be removed daily in order to give free exit for any hidden pockets of serum. In addition, if the crusts become cracked, particularly over joints, a portion of the eschar should be sharply debrided to prevent irritation and infection. These open areas then may be dressed with a thin layer of fine mesh gauze, and sprayed frequently during the day with sterile saline solution. If areas of the crust become softened and bulge, the bulging eschar should be removed by sharp dissection, and the defect covered by fine mesh gauze. This should be sprayed frequently with sterile saline solution, with or without an added antibiotic. Insofar as possible, the eschar should be allowed to remain intact and dry until natural separation occurs. Following natural or mechanical separation and removal of the eschar, if epithelization has not taken place (except for very small areas), skin grafting should be carried out.

IN CASES GIVEN CLOSED OR VASELINE-PRESSURE TREATMENT

The initial care of burn wounds where the closed or vaseline-pressure-dressing technique is to be employed is the same as in the exposure method. After the wounds have been thoroughly dried, single-layer strips of lightly impregnated vaseline fine-mesh gauze are laid over the wounds. These strips are never long enough to encircle an extremity and produce constriction. Dress fingers separately and immobilize the hand. The second layer is of bulky absorbent roller-gauze applied with adequate, even pressure. The third layer is the compressive dressing, usually stockinette cut on the bias, or an elastic-type bandage. The patient is then returned

to his room and properly positioned in bed. If extremities are involved they should be elevated and supported.

These dressings must be applied by the strictest sterile technique. Infection is more likely to develop in burn wounds which are dressed than in those exposed. The dressings are usually removed at the end of one week. At this time reestimation is made as to depth and extent. Many superficial, second degree wounds may be exposed at this time. Others should be re-dressed in exactly the same manner as the first dressing. The second dressing procedure usually takes place at the end of 14 days (post-burn), again in the operating room under sterile conditions. Third-degree burns will be open wounds and require grafting. Dressings should be changed when they become wet and malodorous.

ANTIBIOTICS

All patients with extensive burns should be treated with antibiotics at the earliest opportunity. Penicillin and the tetracyclines appear to be the most effective agents initially. Perineal, gluteal, and thigh burns may be partially protected by the routine administration of sulfasuccidine. If suppuration or septicemia develop, sensitivity studies should direct further antibiotic therapy. Administration of antibiotics to patients with severe burns is mandatory—by intravenous, intramuscular, or oral routes.

NUTRITION

The problems of infection and malnutrition in severe burns are related. A vicious circle may be established with the onset of these complications. When infection develops the appetite leaves, food intake decreases, wound healing and resistance to infection are adversely affected. A diet high in calories, carbohydrates, protein and vitamins (particularly vitamin C) should be given. The caloric intake should be maintained at a minimum of 4000 calories in severely burned adults, if necessary by supplementing oral with tube feedings. For tube feeding, the natural foods will be best tolerated and most effective.

Between completion of skin coverage and institution of reconstructive surgery, physiotherapy is of extreme importance.◀

Nebraska M.J., 43:75-85,1958.

Physiologic Approach to the Treatment of Labyrinthitis

Although the etiology of Meniere's syndrome remains to be established, the underlying factors are gradually being recognized. In the disease, the capillary syndrome with protein leakage and extracellular fluid is present. There appears to be a shift in the electrolyte content of the endolymph, with an increase in the ratio of sodium to potassium. By restoring capillary function and the normal ratio of sodium-potassium in the labyrinth, in non-complicated labyrinthitis a favorable effect is produced.

Nine patients were treated with a low salt diet supplemented with citrus bio-flavonoids. Freedom from symptoms was experienced in from three to six days after institution of treatment.

Miller, T. R., *Eye Ear Nose & Throat Month.*, 37:601-603,1958.

Gastrointestinal Manifestations of Primary Hyperparathyroidism

Evidence of hyperparathyroidism may follow gastrointestinal symptoms manifested many years previously

ARNOLD M. MOSES, M.D., *New York, New York*

Of 37 cases of primary hyperparathyroidism, 26 were in females. Peptic ulcer was proved in four cases, gastrointestinal symptoms were prominent in five, in 28 there were no significant gastrointestinal symptoms.

CASE 1

A 67 year old man was first admitted with abdominal pain, weakness and melena. For 15 years he had felt intermittent abdominal pain which generally responded to belladonna. Gastrointestinal x-rays revealed a projection from the lesser curvature of the stomach, interpreted as a benign gastric ulcer. The patient was treated conservatively and discharged. He was readmitted seven years later because of swelling and pain in the right leg. Occasional melena had been noted. X-rays revealed large cystic areas throughout the long bones, consistent with hyperparathyroidism. Serum Calcium was 9.2 to 11.8 mg. percent, serum phosphorus 1.1. to 1.6 mg. percent, alkaline phosphatase 15.3 King-Armstrong units. Exploration was done and a single parathyroid adenoma removed. The postoperative course was uneventful. Two months later, in an acute attack of abdominal pain, the patient expired. Post-mortem examination revealed a dissecting aneurysm of the thoracic aorta and a healed gastric ulcer. Symptoms of gastric ulcer were present for 22 years before evidence of hyperparathyroidism appeared.

CASE 2

A 39 year old man was admitted because of epigastric distress. He had recurrent renal calculi for 14 years, episodic epigastric burning was relieved by antacids and food. Five years previously hyperparathyroidism had been diagnosed and two parathyroid adenomata had been re-

moved. The patient was asymptomatic for four years when he had a renal calculus attack. At that time the epigastric pain recurred. One year later a duodenal ulcer was demonstrated by x-ray.

At the time of admission serum calcium range was 12.5 to 15.4 mg. per cent, phosphorus serum 0.8 to 1.4 mg. per cent, alkaline phosphatase 5.2 to 8.9 King-Armstrong units. Urine calcium was 400 mg. per 24 hours on a Bauer-Aub diet. X-rays revealed radiating folds in the duodenal bulb with a persistent patch of barium. A large parathyroid adenoma was removed from the anterior mediastinum. The postoperative course was uneventful, with normal calcium and phosphorus.

The parathyroid adenomata were an interesting feature in this case. This has been reported in 8 per cent of cases of primary hyperparathyroidism, along with what appears to be a direct relationship between ulcer symptoms and parathyroid overactivity.

CASE 3

A woman was admitted because of epigastric pain. She had transient episodes of abdominal pain many years previously and later a duodenal ulcer was demonstrated by x-ray. Just prior to admission severe epigastric pain developed, radiating to the back. This was accompanied by episodes of nocturnal vomiting. Ten years previously she had severe left flank pain radiating to the groin. Renal calculi were suspected but no x-ray studies were made. Six years prior to this hospitalization a swelling of the right wrist was noted, and one year later a cyst was removed from the os hamatum which proved to be a giant-cell tumor. A 2 cm. non-tender nodule appeared in the left lobe of the thyroid. Serum calcium was 11.9 to 13.7 mg. per cent, serum phosphorus 1.2 to 4.2 mg. per cent and alkaline phosphatase 5.9 to 9.1 King-Armstrong units. The 24-hour urine calcium on a Bauer-Aub diet was 111.5 mg. Intravenous pyelogram was normal. X-rays revealed some demineralization but no characteristic lesions of hyperparathyroidism. An ulcer crater was visualized on x-rays.

A left hemithyroidectomy was performed. The excised specimen contained a cystic parathyroid adenoma. Postoperative serum calcium was normal. She manifested no further G.I. symptoms. Symptoms of duodenal ulcer preceded probable renal calculus by 16 years, definite hyperparathyroidism by 26 years. The persistent vomiting at admission was probably due to hypercalcemia *per se*.

CASE 4

A 46 year old woman was first seen with a history of renal calculi for 20 years and a left nephrectomy. For 10 years she had intermittent epigastric discomfort relieved by sodium bicarbonate. There was no history of excessive milk ingestion. X-rays revealed an ulcer crater, bone was normal. At that time blood urea nitrogen was 33 mg. per cent, serum calcium 12.6 to 13.8 mg. per cent, serum phosphorus 2.0 to 2.6 per cent. On a Bauer-Aub diet, the 72-hour urinary calcium excretion was 586 mg. Parathyroidectomy was advised but refused. Progressive uremia developed and the patient died.

DISCUSSION

In most cases of peptic ulcer with hyperparathyroidism the ulcer is duodenal, but gastric and esophageal ulcers have been reported in the middle aged and elderly. Females with primary hyperparathyroidism outnumber males 2.2 to 1, yet in the male complicating peptic ulcer is twice as frequent as in the female.

It has been estimated that 16 per cent of males and 4 per cent of females in the general population are afflicted with peptic ulcer at some time in their lives. Gastrointestinal symptoms in hyperparathyroidism, whether or not associated with demonstrable peptic ulcer, have markedly improved almost without exception after parathyroidectomy. In the few cases in which such symptoms have not cleared, other adenomata have been postulated. The medical treatment of peptic ulcer complicating hyperparathyroidism has the inherent danger of precipitating acute parathyrotoxicosis and of calcium salt deposition in the urinary tract.◀

J. Mt. Sinai Hosp., 25:339-345,1958.

Demonstration of Neutralizing Antibody in Gamma Globulin and Re-evaluation of the Rubella Problem

15 ml. of gamma globulin given before exposure to rubella provided immunity to a group of 300 men

SAUL KRUGMAN, M.D., and ROBERT WARD, M.D.,
New York, New York

The association of rubella in pregnancy with congenital malformations, still-births and abortions is now common knowledge. Maternal rubella infection may be followed by congenital cataracts, deafness, microcephaly, mental retardation and congenital heart disease—singly or in combination.

It has been postulated that rubella virus damages the fetal tissues that are multiplying most rapidly at the time of infection. Rubella acquired after the first trimester of pregnancy imposes no added risk to the infant *in utero*.

GAMMA GLOBULIN STUDIES

Studies on the prevention of rubella with gamma globulin have yielded findings ranging from significant protection to none at all. These results prompted the authors to test for the presence of neutralizing antibody in ordinary gamma globulin, convalescent rubella plasma and gamma globulin prepared from plasma of patients convalescent from rubella.

These studies demonstrated the presence of neutralizing antibody for rubella virus in the tested samples of ordinary gamma globulin, convalescent-phase plasma and convalescent-phase gamma globulin.

Since gamma globulin is prepared from pooled adult plasma, the concentration of the antibody will reflect the immune status of the donors of the plasma pool. Some young adults are more susceptible to rubella than to measles. The concentration of rubella antibody in gamma globulin must be lower than that of measles antibody.

A group of 900 recruits at a military installation were inoculated shortly after arrival at the base. Three hundred men received 15 ml. of gamma globulin intramuscularly, 300 received 5 ml., and 300 received saline solution. A total of 10,732 men at the camp received nothing. Shortly afterward an outbreak of rubella was in progress. The attack rates per 1,000 in these 4 groups of men were 15.7 for the group receiving nothing, 23.3 for the saline controls, 6.7 for the group receiving 5 ml. of gamma globulin, and 0 for the group receiving 15 ml. of gamma globulin.

RESULTS

From this and other like studies it appears that passive protection against rubella can best be achieved by early administration of large doses of gamma globulin. Future controlled field studies will have to define the precise dosage. In the meantime, gamma globulin in a dose of 0.15 ml. to 0.20 ml. per pound of body weight appears to be indicated. It has been our practice to give 20 ml. intramuscularly to women exposed during pregnancy. If convalescent-phase rubella gamma globulin is available, 10 ml. given intramuscularly should suffice.

RISK OF CONGENITAL MALFORMATION

The early estimates of 90 or more per cent were derived from retrospective studies, which originated with the damaged infant. The normal infants, therefore, did not come to the attention of the observers. In recent years a number of surveys of the prospective type have been reported. These studies have originated with the rubella infection in the pregnant woman, and have ended with the newborn infant—normal or abnormal. The accumulated data indicate that maternal rubella infection in the first trimester may be followed by congenital malformations in 10 to 12 per cent of cases.

Under the conditions of a recent study there was a 6:1 ratio of congenital malformations after rubella in the first trimester, as compared with uncomplicated pregnancy.

MANAGEMENT OF RUBELLA IN PREGNANCY

In case a woman has been exposed to or has contracted rubella in the first trimester of pregnancy, the physician must decide whether to give gamma globulin on exposure, or whether to recommend a therapeutic abortion if the disease occurs.

The administration of gamma globulin to a person exposed to rubella may have no effect, prevent the disease, or modify the rubella so that a rash does not develop. Earlier studies demonstrated that rubella can occur without a rash and that a viremia occurs in this condition. Thus, an inoculation of gamma globulin may give one a false sense of security.

Nevertheless, it is desirable that all pregnant women with no previous history of rubella be given at least 20 ml. of gamma globulin intramuscularly in the first trimester, as

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soon after exposure as possible.

This is for possible beneficial effect of the early administration of large doses of gamma globulin. Recent prospective surveys show that the risk to the fetus after maternal infection is not as high as earlier reports suggested. If rubella convalescent-phase gamma globulin is available, 10 ml. administered intramuscularly should be adequate.

MANAGEMENT OF THE PREGNANT WOMAN WHO HAS CONTRACTED RUBELLA

A pregnant woman for whom there may be a religious or other contraindication to abortion will be permitted to go to term. The same decision could be made in an elderly, childless couple whose chances of having children in the future are small. When it is evident that a therapeutic abortion is neither advisable nor possible, it is incumbent upon the physician to reassure the parents. He should acquaint them with the recent reports of the prospective studies indicating that most cases of rubella in pregnancy are followed by births of normal infants.

On the other hand, the risk that a woman will give birth to a deaf, blind or mentally defective infant is increased sixfold if rubella develops during the first trimester of pregnancy. A young woman in her early childbearing period, with no religious or other contraindications to abortion, should have a therapeutic abortion if there are no legal obstacles.

EXPOSE YOUNG GIRLS TO RUBELLA

At the present time the prevention of congenital malformation caused by rubella can be best achieved by deliberate exposure of young girls to the disease. In this manner they may acquire a durable immunity that will protect them during their childbearing period.◀

New England J. Med., 259:16-19,1958.

One Hundred Colon Cancers

Some suggestions are made for the pre- and post-operative care of colon carcinoma

JAMES F. BISHOP, M.D., *Davenport, Iowa*

Three factors make carcinoma of the colon a disease of significance: It is a common cancer, it usually is easily diagnosed, and its survival rates are better than those of most cancers. Surgery was undertaken upon 100 persons who had carcinoma between the cecum and the anus.

Of these cancers 97 were adenocarcinomas, one was a squamous-cell lesion of the anus, and two other squamous-cell cancers were seen during this period. These 100 patients had 115 operations, and there were five surgical deaths. Of the 100 cancers, 60 were rectal, 36 were in the sigmoid. The majority of large-bowel cancers are within reach of the 10-inch sigmoidoscope.

The patients were 51 males, 49 females, two-thirds of them in their 50's and 60's. Since this series a 15 year old boy was operated on for carcinoma of the descending colon with widespread lymphatic metastases, and died six months afterward.

DIFFERENT FORMS OF CANCER

Cancer of the colon may be in several forms. The fungating, polypoid lesion of the right colon and the annular, ulcerated neoplasm of the left are the most common. Either lesion may appear in either half of the colon. The fern-like papilloma usually has carcinoma within its depths, a pedunculated polyp and even a match-head-sized sessile polyp may show invasion.

EXTENSION

These tumors involve surrounding structures by infection and direct invasion. Metastasis is most likely to be to regional or blood-borne to the liver. In this group there were found a nodule astride the optic chiasma, cervical and axillary metastases, masses in the lungs, and a subcutaneous nodule over the sternum.

SYMPTOMS AND DIAGNOSIS

The most common symptom was rectal bleeding as gross blood, bloody mucus, or both, in all but a few instances, preceded by changes in bowel habit, excessive flatulence and pain. Suspicions may be easily verified by biopsy, when within reach of the sigmoidoscope. Some patients cannot—or will not—tolerate the scope to its limit. Under these conditions three or four inches of sigmoid are not visualized in an area where x-ray evidence is undependable and where cancer is common. By sigmoidoscopy under anesthesia lesions have been found which otherwise would not have been detected. X-ray differentiation between cancer and diverticulitis is usually easy, sometimes difficult, occasionally impossible.

TREATMENT

The treatment of cancer of the colon is surgical, and is divided into prophylaxis, palliation and attempts at cure. Preoperative preparation includes the correction of anemia and deficiencies in fluid, proteins and electrolytes. A number of effective bowel antiseptics are available for preoperative prophylaxis.

Prophylactic surgery includes excision of rectal or colonic polyps, whether single, multiple, or present as familial polyposis.

A rectal polyp may be of low-grade malignancy, and it is safe to observe such a site of removal at intervals, rather than inflict abdomino-perineal resection. Polyps within the colon are best treated by segmental resection, which is a safer procedure than polypectomy. Prophylaxis must also include excision of scarred, pseudopolypoid colons following long-standing ulcerative colitis.

In 15 patients of this group, colostomies, resections and short-circuiting procedures were done for palliation, since distant metastases—usually to the liver—had made the disease incurable.

When at all possible, the primary lesion should be removed, even when it means an abdomino-perineal resection. Except in the presence of obstruction, there is little palliation in a colostomy which leaves behind an infected, ulcerated neoplasm. These are radio-resistant growths, but deep x-ray therapy often relieves pain and is valuable palliation.

DIAGNOSE EARLY AND EXCISE RADICALLY

Early diagnosis and radical excision are again emphasized. As much as possible of the regional node-bearing mesentary and a generous portion of bowel tube above and below the lesion should be removed. In left-side lesions, this assumes ligation of the inferior mesenteric artery at the aorta, and the inferior mesenteric vein where it passes beneath the ligament of Treitz.

Since blocking of regional nodes by tumor may direct the flow upward or downward in lymphatics, there is reason to urge even more radical resections of bowel and mesentery. Sometimes procedures are performed whose results do not justify the mutilation.

These operations preserve life, but they leave the patient little chance of really living. We should examine again and again our right to use our modern knowledge to deny the hopelessly ill patient the surcease of death.

DETAILS OF MANAGEMENT

In this series, the operations done in hope of a cure include 40 abdomino-perineal resections. The rest were anterior or segmental resections. In a few selected cases—usually poor surgical risks with large papillary neoplasms, apparently non-invasive — a local approach to rectal lesions was useful. Easy access to the mid- and upper-rectum can be gained by dividing the posterior midline up to the tip of the coccyx, including complete division of the sphincters. An alternate approach is through the bed of the coccyx and the posterior rectal wall. If preceded by adequate preparation and if properly repaired, both incisions heal well without incontinence.

Obstruction, when present, is far more likely to be due to a left-side lesion. Although cecostomy is less shocking in the desperately ill, right transverse colostomy is generally preferable, since it provides better decompression and permits more effective irrigation of the distal segment.

Attempted resection in the presence of obstruction is unwise for two reasons: The disturbances in chemistry and physiology resulting from the obstruction increase the risk, and the dilated bowel makes adequate mobilization difficult if not impossible. With obstruction relieved, preparation for definitive surgery can be carried out, and resection can be done with relative safety, usually 10 to 14 days later.

After abdomino-perineal resections, all the perineal wounds were left open widely, and the packing was removed on the third to the fifth day. Sitz baths two or three times daily thereafter contribute to comfort, cleanliness and healing. These wounds heal completely in from two to six months.

Other postoperative measures in these bowel operations include intravenous glucose in water until oral feeding is begun. Because the adrenals hold salt following surgical trauma, saline is not given for the first three days, and thereafter only if gastric suction is required.

ABOUT ILEUS

Ileus apparently is a physiologic mechanism of defense, and cessation of peristalsis seems to be defensive in two ways. First, by preventing further extrusion of intestinal contents into the peritoneal cavity through a perforation or injury, second, by avoiding the gross movement of intestinal loops which would tend to spread infection. One cannot expect the gastrointestinal tract to differentiate between the insult of a perforated appendix or peptic ulcer, on the one hand, and injury to its integrity by surgical assault, on the other. It defends itself in the same manner under both circumstances. When the damage and the threat seem to be subsiding, the digestive tract resumes its activity—cautiously at first, and then with full confidence.

Some surgeons send patients to the operating room with the nasal tube in place, and apply suction for a variable length of time postoperatively. When, about the third day, the patient begins to pass gas, the surgeon pulls out his tube, delighted because he has "cured" his patient's ileus. He

has done nothing of the sort since the irritation of the tube only adds to the patient's immediate postoperative burdens. Of 100 people in this series who underwent abdominal operations on the colon, 73 did not require gastric suction at any time, 27 not until at least 48 to 72 hours after surgery, and then in many instances only for 12 to 24 hours.

Stimulants are seldom used to encourage bowel activity for two reasons: First, a reluctance to place undue stress upon an anastomosis, and second, the possibility that the ileus may have resulted from a localized peritonitis. In a rare instance, ileus may persist for seven days or so, and obstruction may be suspected. In the absence of cramping, obstruction is unlikely, and watchful waiting is rewarded by a return of bowel function.

RECOVERY DELAYING FACTORS AND COMPLICATIONS

Among factors delaying recovery are prolonged operating time, rough handling of the viscera, leakage or infection in the area of repair, and the effects of chronic anxiety.

Complications in these 100 cases include seven wound infections of varying severity, seven instances of thrombophlebitis, and four wound disruptions.

RESULTS

Of the patients operated upon for a cure, 24 had reappearance of their cancers in from four months to 2½ years. In no instance has the tumor reappeared later than 2½ years after surgery.

Three have died cardiovascular deaths after having survived four or more years free from disease.

Some others, including a suicide, were apparently free from disease at the time of death from other causes.

Of 68 patients operated upon four or more years ago in hope of a cure, 42 lived at least four years. Thus the four-year survival rate is 62 per cent.

J. Iowa. M. Sc., 48:135-139,1958.

Diabetic Coma in Infancy

During infancy, diabetes mellitus presents itself as an acute metabolic disturbance. Between 1925 and 1946 the mortality averaged 45 to 50 per cent for collected cases of diabetes in infants under one year; in more recent series the mortality has been nearer 25 per cent.

Admission diagnoses in the 12 most recent cases of diabetes under one year were pneumonia in four, meningitis in four, dehydration and infection in one, "shock" in one and diabetes in one. Reported cases in this age group are rare, and it is suggested that cases may masquerade as meningitis or pneumonia.

In those cases with a severe ketonemia the pH, even with adequate respiratory compensation, may fall below 7.2.

Best control is achieved when insulin is given in dosage based on the results of 4-hourly blood-sugar and keto-acid estimations.

The history of familial incidence may be over 40 per cent where accurate information is available. The importance of parental intelligence and cooperation in subsequent management is stressed.

Beaven, D. W., *Brit. M.J.*, 2:198-201,1958.

Iatrogenic Disease and Anesthesia

Drugs which do not appear to have side-effects on the conscious patient may unexpectedly complicate anesthesia

JOHN W. DUNDEE, M.D., *Belfast, Ireland*

SULPHONAMIDES

Sulphonamides were probably the first drugs that were thought to influence the effects of anesthetics. They were said to intensify cyanosis and increase the toxicity of the thiobarbiturates, but this is no longer believed.

METHONIUM AND A CONGENER

In 1951 anesthetists were warned to be aware of patients who were being treated with methonium. At that time these compounds were being widely used as therapy for peptic ulceration, and had the ulcer perforated in such a patient he would have been in a very grave pre-operative condition. The hypotensive effect of the methonium compound is more marked in the anesthetized than in the conscious subject, and the hazard of anesthesia in patients receiving these drugs is obvious. It is to be expected that patients receiving mecamylamine are liable to the same changes in the blood pressure during anesthesia as patients on hexamethonium.

RAUWOLFIA AND ITS DERIVATIVES

Rauwolfia is not a ganglion-blocking drug, but causes hypotension by central depression of the vasomotor system. The lassitude and drowsiness which it causes suggest that it may potentiate narcotics. Of 40 cases receiving rauwolfia therapy, 40 per cent had a fall in blood pressure of more than 40 mm. Hg. and a pulse

rate below 60. The hypotension responded in a variable manner to vasopressors; relieving the bradycardia with atropine was of help. Rauwolfia potentiates ganglion-blocking drugs and produces nasal congestion and excess salivation. There may be difficulty in maintaining a clear airway, and the risk of excessive bleeding after nasal intubation is increased. Rauwolfia has a slow onset of action, and its effects last for several weeks. Where possible the drug should be stopped two weeks before operation.

VERATRUM

The effect of veratrum alkaloids is a reflex fall in blood pressure and pulse rate. This can be very confusing when it occurs in the anesthetized subject.

It can be seen that all drugs currently used in the treatment of hypertension can affect the course of anesthesia. It is essential that the anesthetist know well in advance of the operation when such drugs are being given, and on occasion surgery should be postponed until their effects have worn off.

PREOPERATIVE PREPARATION IN ADRENAL INSUFFICIENCY

A review of reported anesthetics to patients with Addison's disease reveals that of 18 cases with no special pre-operative preparation 89 per cent developed hypotension and the mortality was 56 per cent. In comparison, hypotension occurred in only 55 per cent of 20 patients who received specific hormone therapy and there was no mortality associated with the anesthesia. This applies to all types of adrenal failure, including that caused by inhibition of the pituitary by cortisone or corticotrophin. Corticotrophin stimulates the cortex to produce an excess of cortisol, which in turn causes pituitary inhibition. After these substances have been withdrawn the pituitary-adrenal axis may take several months to recover normal function.

In adrenocortical insufficiency, patients react to the stress of anesthesia and surgery by hypotension (out of proportion to the blood loss), respiratory depression and delayed recovery. Manipulation of a joint, reduction of a dislocated shoulder, or dilation and curettage, have been followed by profound hypotension in patients with pituitary failure. To patients already receiving cortisone or corticotrophin, an increased dosage should be given before operation. In patients who have stopped treatment within six months of surgery the problem is greater, especially in emergency cases where it may not be known that such drugs have been used.

Preoperatively all patients should be questioned regarding steroid therapy. Therapeutic doses do not interfere with wound healing.

TRANQUILIZERS

A recent article estimates that 50 million pounds of tranquilizers were sold in the United States in 1956. In modifying response to anesthesia the phenothiazine derivatives are the most important group, and the effects of chlorpromazine have been studied in detail. Other members of this series vary in their action in degree only, and possess the same hazards as chlorpromazine.

Long-term use continued to the time of induction of anesthesia can greatly prolong the duration of action of both narcotics and relaxants. The drug itself can cause hypotension and tachycardia, both increased by the

head-up tilt and in the presence of hypovolemia. Like the methonium compounds, it potentiates the hypotensive action of thiopentone. Because of its adrenolytic action, one would expect a severe fall in blood pressure in patients who have received chlorpromazine before ether anesthesia.

Tachyphylaxis to the hypotensive effects of chlorpromazine follows its prolonged use. This is important when the drug is used as an adjuvant in the production of hypothermia by surface cooling. The long-term use of chlorpromazine also seems to induce resistance to ganglion-blocking drugs.

HAZARDS OF ASPIRATION

Of 589 fatalities associated with anesthesia, the largest single cause of death was regurgitation and vomiting followed by aspiration. Of the 110 deaths from this cause, 70 per cent occurred in surgical emergencies, but six deaths followed oral glucose solution, given pre-operatively to diabetics, being regurgitated or vomited. On five of these the operation to be performed was trivial. Water passes rapidly into the duodenum, but hypertonic glucose solution prolongs the emptying time of the stomach.

Apart from the report of 15 deaths from vomiting or regurgitation during delivery, there have been many publications drawing attention to this hazard. The inhalation of liquid material can cause an asthmatic type of attack, with bronchospasm, pulmonary edema and cardiac failure. Death usually occurs within 36 hours of delivery. The greater use of local analgesia, abandonment of the lithotomy position, and the routine passage of wide bore stomach tubes before induction of anesthesia have all been recommended. The answer probably lies in appreciating that absorption from the intestine is disturbed during parturition.

CITRATE INTOXICATION

Citrate intoxication should be suspected if there is a poor response to apparently adequate blood transfusion, especially in patients with liver disease, during hypothermia, or where the hepatic circulation has been temporarily occluded.

DRUG INFLUENCE ON RESPONSE TO ANESTHETICS

Attention is drawn to the increasing use in medicine over the past few years of drugs which influence the response of patients to anesthesia. This side-action cannot usually be predicted and in most cases it has been detected by chance after the preparation in question had been in clinical use for years. In all the instances reported here the effect was to engender an increase in toxicity of one or more of the effects of general anesthetics.

Agents whose main effect is to decrease vascular tone, such as the ganglion-blocking drugs or chlorpromazine, if given before anesthesia, increase the hypotensive action of the narcotics, and severe and even fatal collapse may follow what are considered to be normal doses of anesthetic drugs. This applies particularly to the intravenous barbiturate anesthesia. Care must also be taken in anesthetizing patients who are receiving rauwolfia, veratrum alkaloids or mecamylamine.

Phenothiazine derivatives prolong the narcotic action of anesthetics. This also seems to apply to the non-phenothiazine preparations which are used for the control of tremor in Parkinsonism, and possibly may be a side-effect of all tranquilizers.

A dangerous degree of respiratory depression can result from the combination of analgesic drugs and the intravenous barbiturates. A similar result can occur when cyclopropane is administered to patients who have had deep x-ray therapy to the head and neck.

THE STEROIDS

Induced adrenocortical insufficiency following the prolonged use of cortisone, its analogues, and corticotrophin, makes patients sensitive to the stress of surgery and anesthesia. Prolonged severe hypotension, respiratory depression, and delayed recovery may follow surgery in such patients. These undue effects respond rapidly to intravenous cortisol, but prevention by increased pre-operative dosage of cortisone and corticotrophin is preferable. Increasing use of the steroids is focusing attention on this hazard, and especially so in minor cases where one does not normally associate any risk with anesthesia. It must also be stressed that steroid-induced primary pituitary failure may persist for several months after stopping the drugs.

CONCLUSION

The hazards of inducing anesthesia in patients with a full stomach are now widely appreciated, and for this reason the pre-operative preparation of diabetic subjects with oral glucose is deprecated. Other problems which anesthetists may encounter are the incompatability of pitocin with light cyclopropane anesthesia, and the possibility of citrate intoxication as a differential diagnosis for cardiovascular collapse after massive transfusion of stored blood.

In very few of the cases reported did the anesthetist know of the use of various drugs before operation, or associate hypotension or prolonged unconsciousness with any form of routine medical treatment.◀

Brit. M.J., 1:1433-1438,1958.

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many business men. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

Although it is not apparent to outsiders, the course of business growth is not always smooth and uninterrupted. Companies, even the biggest of multi-million dollar corporations, do make mistakes or run into various business problems and occasionally run into periods where profits are hard to come by. Indeed, the U.S. economy as a whole is not immune to recessions, as the experience of the past 18 months has shown.

Nonetheless, such periods often offer the biggest opportunities for capital gains that investors are likely to come upon. There is actually an entire school of investors who believe in "buying 'em when nobody likes 'em"—buying stocks that are out of

favor at the moment because of some type of problem besetting a company or industry. Other investors seek stocks to buy among the list of stocks which hit new lows for the year on any given day.

The course of the stock market during the past two years lends some credence to the thinking behind these theories, if not to the mechanical details of their operation. The Dow-Jones Industrial Average, widely used to indicate the level of the market as a whole, fell from a peak of 521 in the Summer of 1957, when the recession got under way, to a low of 416 in the Fall of that year. With many months of the recession still ahead, the business outlook wasn't particularly encouraging at that point, and earnings prospects for many issues seemed poor. That level was the low point for the recession, and the stock market has since climbed to a new all-time peak of close to 550 on the Dow-Jones average.

Obviously this approach to investing, like any other technique, has pitfalls. Companies don't always solve their problems and surge to new levels of profitability. But when they do, major capital gains are a possibility. This month we are discussing three companies which we believe are well on their way toward solving just such a major problem.

The first, Acme Industries, is a small producer of air conditioning components which is going through the difficult process of changing its marketing emphasis from primarily selling components to other, bigger air conditioning manufacturers into a producer both of components and of its own brand items to industry. The second, Wallace & Tiernan, is a medium-sized firm now on the threshold of successfully overcoming the difficulties of introducing a major new product line which is, in turn, a new type of process—introducing automation to breadbaking. The third, Olin Mathieson, is a huge, widely diversified industrial enterprise which we think is now on the road to an eventual profit recovery and more generous evaluation in the financial community.

ACME INDUSTRIES

The shares of Acme Industries, selling at little more than nine times fiscal 1958 earnings, appear attractively priced for capital gains possibilities. We believe the company stands at the threshold of a major advance in both sales and earnings. The transitional problems in changing the direction of sales emphasis from components to the company's own brand name appear to have been solved. What's more, the major expansion program completed approximately a year ago is now paying off in wider operating profit margins and much larger potential capacity.

Until a few years ago Acme Industries was primarily known as a manufacturer of cooling components for sale to other major air conditioning firms, which then integrated them into their own systems. However, in the fiscal year just ended, more than half the company's sales were their own brand items. Furthermore, the company has stated that it will emphasize the sale of complete air conditioning systems to a much greater degree in the future than ever before.

To achieve this greater emphasis on their own field sales, the company last year tripled its sales representation. Moreover, whereas Acme formerly had multiple line representatives in

danger signals in office practice

decisions *were* his business

The first warning of mental or emotional disturbance may come when a patient suddenly becomes confused and irascible after a lifetime of calm, decisive thinking. But progression to a more serious condition is not inevitable. The episode can often be aborted with early Pacatal therapy.

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many of its outlets, it now has full time single line representation. Sales representatives are now located in 75 cities in the United States and five in Canada. In many of these cities, additional personnel have been added to the selling force.

To supplement the strengthened sales force, in September the company introduced new product lines and improved designs in its existing products. A new packaged water chiller line from three to 125 tons was introduced, 50 per cent smaller than the old models of the same capacity, and a self-contained packaged air conditioner in sizes from 20 to 60 tons was introduced that requires only power, water and drain hook-ups. Also introduced were new heating and cooling coils for all applications, smaller packaged air conditioners, such as the type used in restaurants and stores, new remote room units, air-cooled condensers and air handling units.

The redesigned packaged liquid chiller mentioned represents one of the newest developments within the air conditioning industry. Since they require less floor space and support and are simpler to install, they are of particular advantage in many applications where space is limited.

In addition to the new products, of course, Acme will continue to manufacture components. Components are now sold to such major air conditioning companies as Carrier Corporation and the Airtemp Division of Chrysler Corporation.

A recent trade journal study points out that more than 80 per cent of factories and commercial buildings in the United States have no form of air conditioning at all. The relative use of air conditioning in existing buildings is so small that a large potential for the industry can be projected far into the future. However, the only satisfactory manner in which many old buildings can be air conditioned, either because of space limitations or structural design, is through the use of packaged units. Industrial applications for the packaged units include the plating and anodizing industries, as well as the food freezing, electronic, chemical and petrochemical industries. Acme, now offering a complete line of packaged units, is in an excellent position to capitalize on this potential.

Toward the middle of fiscal year 1957, the company completed its new manufacturing plant in Jackson, Michigan. With more than three acres of floor space, this plant nearly doubled the area available for production. Fabrication and assembly of several classes of products have been transferred from Acme Industries' other plant in Jackson to these new facilities. In turn, this has permitted a more efficient arrangement of all manufacturing operations.

For the fiscal year ended July 31, 1958, the company's net income came to $291,000 or 76¢ a share, down from a net income of $340,000 or 89¢ a share in 1957, and $384,000 or $1.00 per share in 1956. The decline in net in 1957 can be attributed to the start-up and moving expenses incurred during the erection of a new plant late in that fiscal year, and the 14 per cent decline in the fiscal year just ended was the direct result of a similar 14 per cent drop in sales due to the recession.

Sales for fiscal 1959 are expected to be substantially above the $8 million reported in 1958. We believe sales will be between $11 and $13 million, with both field and component sales contributing to the increase. The in-

Acme Industries			
Price	7½	Capitalization (7/31/58)	
Indic. Dividend	20¢	Long-term Debt	$850,000
Yield	2.7%	Common Stock	382,791 shs.
Traded	O.T.C.		

ventory liquidation of the last 12 months in the air conditioning industry appears to have run its course. Thus Acme's component sales should increase substantially even if total industry sales volume stays at the same depressed levels of last year, and should increase at a much faster rate if the industry resumes its long-term growth pattern this year and begins to build up inventories again. Management of the company feels that an annual sales level of approximately $15 to $18 million will be reached some time before 1960.

With the higher efficiency and closer cost control of the new plant, we believe earnings for fiscal 1959 should range between $1.25 and $1.75. Dividends have been on an annual 20¢ rate since January, 1957 when the dividend was placed on a quarterly basis. This cash disbursement was supplemented by a 5 per cent stock dividend in February of 1958. With a strong financial position (a current ratio of 4.3 to 1), increases in the cash dividend rate can be expected as earnings increase.

WALLACE & TIERNAN

Wallace & Tiernan Inc. is another example of a company about to take a big step forward through the solution of a problem—in this case, the problem of successfully developing and introducing a major new process which will introduce automation to the baking of bread. Through this Do-Maker process, the company will also be solving the problem of inefficiency for many small baking companies.

Wallace & Tiernan basically is a well established, medium-sized company, deriving some two-thirds of sales from chemicals and pharmaceuticals, with the remainder stemming from industrial equipment and instruments. The company's largest division, the Harchem division, with plants at Dover, Ohio and Toronto, Canada, manufactures fatty acids and plasticizers for use in the rubber, textile, soap, plastics, cosmetics, nylon and other industries. The company's Lucidol division, with plants at Tonawanda and Genesee, New York, Fort Erie, Canada and Wasserburg, Germany, manufactures organic peroxides used as catalysts in polymerizations, drying accelerators, oxidizing agents and bleaching agents.

The Maltbie Laboratories division, operating plants at Belleville and Hanover, New Jersey, and Toronto, Canada, manufactures ethical pharmaceuticals including *Desenex, Caldesene, Nesacaine* and the *Cholan* products.

The company has two process divisions. The flour service division, with research and customer service laboratories at Belleville, New Jersey, Tonawanda, New York, and Chicago, Illinois, supplies equipment, chemicals and technical services to the flour milling industries for the maturing, bleaching and enrichment of flour. The Decco division, with customer service laboratories in Monrovia, California, and warehouses in cities throughout major produce areas, serves the fresh fruit and produce industries. Decco wash and gas treatment processes are used to prevent bacterial and fungal spoiling of celery,

peppers, asparagus, and melons.

The company also has two equipment divisions. The Chlorinator and Feeder division, with plants in Belleville, New Jersey, Toronto, Canada, London and Tonbridge, England and Wasserburg, Germany, manufactures chlorinators and chemical feeding apparatus widely used for municipal water and sewage treatment, swimming pool sterilization, industrial waste and process water treatment and materials handling. The company's instrument division produces sensitive pressure instruments such as barometers, altimeters, and various aids to navigation such as buoys, lanterns and foghorns.

Subsidiaries of the company include the Electro Rust-Proofing Corporation, which furnishes equipment and services for cathodic protection—a means of inhibiting the electrochemical action that causes rust and corrosion on ships. Another subsidiary, the American Machinery Corporation, manufactures produce handling equipment.

It is essentially these activities which have resulted in a commendable record of operational achievements in recent years. Sales in the five-year period between 1952 and 1957 rose 36 per cent, while earnings per share expanded by almost 69 per cent, from $1.53 to $2.58 last year. Both pre-tax profit margins and return on invested capital, which reached 14.1 per cent and 14.5 per cent in 1957, have been improving in recent years, contrary to the experience of this industry generally. Moreover, the company's financial condition is very strong, its current ratio being 3.2 to 1, with only an insignificant amount of long-term debt outstanding.

While the company's record is reason enough for purchase of the shares, there exists an additional, relatively new element of decided interest, in terms of eventual added earning power. Wallace & Tiernan has been working for several years, through a subsidiary known as the Baker Process Company, on a patented process designed to introduce a high degree of efficiency through automation in the baking of bread. Called the Do-Maker process, the equipment is said to reduce sharply the time required to bake bread, the space required to produce it and the labor costs, at the same time improving quality. The new method of making bread continuously operates at rates up to 4,000 loaves per hour.

After selling only seven installations of the Do-Maker in 1957, the company now estimates that 1958 sales will total thirty units, with sizable increases foreseen next year. The total market for the Do-Maker, both in the United States and abroad, is estimated eventually at about 2,000 machines. Considering that each installation sells for $120,000, it becomes readily apparent that a large new source of earning power may be at hand.

Earnings in 1958 probably will be down somewhat from last year's $2.58, possibly dipping to between $2.00 and $2.25 because of the recession. Earnings for the first half of 1958 dipped to $0.87 a share from $1.23 in the first half of last year. Nonetheless, we feel that earnings in 1959 will show good recovery, and believe the shares are attractively priced for long-term capital gains.

OLIN MATHIESON CHEMICAL CORPORATION

After an extended period of recommending a standstill position regarding the shares of Olin Mathieson, in

Wallace & Tiernan			
Price	31	Capitalization (12/31/57)	
Dividend	$1.40	Long-term Debt	$510,199
Yield	4.5%	Common Stock	1,333,245 shs.
1958 Price Range	33¾-24		
Traded	A.S.E.		

anticipation of severe adversities which eventually materialized, we are now of the opinion that while the company's problems are far from entirely resolved, the current price of the shares almost fully discounts these adversities. The dividend has been cut in half, earnings have deteriorated sharply and company management has come under widespread criticism. The recent recession, plus the mis-timing of a major capital expenditure program with its attendant heavy start-up expenses and unproductivity of new capital, have been key elements in the company's recent difficulties. However, the stage now seems set for eventual recovery once the heavy investment in the new plant begins to show some return, even if only modest, instead of the losses that characterized 1958. Purchase of these shares is accordingly recommended in risk type accounts seeking material gains over a two to four year period.

Olin Mathieson is a highly diversified industrial enterprise which assumed its present form through the merger in 1954 of Olin Industries, Inc. and Mathieson Chemical Corporation, both of which originated in 1892. Olin originally engaged in the manufacture of explosives and ammunition. It entered the metals business shortly before World War I, and became a leading manufacturer of sporting firearms and ammunition in 1931 with the purchase of the Winchester Repeating Arms Company, makers of "the rifle that won the West."

Olin's broad experience in cellulose-based explosives, and in cellulose chemistry generally, led to its entry into the cellophane industry in the years following World War II under DuPont licenses, and then to the acquisition in 1949 of a leading producer of cigarette paper and other fine papers located at Pisgah Forest, North Carolina, where Olin's first cellophane plant was constructed. To provide a permanent supply of pulp wood for cellophane and other cellulose-based products, Olin in 1952 acquired Frost Lumber Industries, Inc., a producer of southern pine and hardwood lumber, which owned approximately 435,000 acres of timber land in Arkansas, Louisiana and Texas, together with saw mills and related facilities. As an adjunct to its continuing interest in ammunition, Olin entered the field of powder-actuated tools later in 1952.

Prior to 1948, Mathieson Chemical was primarily a regional alkali producer but between 1948 and the merger with Olin in 1954, Mathieson engaged in a program of expansion and development which led to a broader position in basic inorganic chemicals, the production of organic chemicals based on natural gas and coal, the production of fertilizers, pesticides and other agricultural chemicals, and a major place in the drug manufacturing industry.

In 1949, Mathieson became an important producer and distributor of sulfuric acid, sulfur, fertilizer and other agricultural chemical products, and in 1951 leased a plant at Morgantown, West Virginia from the U.S. Govern-

all cold symptoms

New timed-release tablet provides:

...the superior decongestant and antihistaminic action of Triaminic

...non-narcotic cough control as effective as with codeine, but without codeine's drawbacks

...an expectorant to augment demulcent fluids

...the specific antipyretic and analgesic effect of well-tolerated APAP

...the prompt and prolonged activity of timed-release medication

Each* TUSSAGESIC *Tablet contains:

TRIAMINIC®	50 mg.
(phenylpropanolamine HCl	25 mg.;
pheniramine maleate	12.5 mg.;
pyrilamine maleate	12.5 mg.)
Dormethan (brand of dextro-methorphan HBr)	30 mg.
Terpin hydrate	180 mg.
APAP (N-acetyl-para-aminophenol)	325 mg.

To reduce upper respiratory congestion and irritating secretions.

For non-narcotic control of the cough reflex.

To augment demulcent respiratory secretions.

For specific, highly effective antipyresis and analgesia.

Tussagesic Tablets provide relief from *all* cold symptoms in minutes, lasting for hours.

Dosage: One tablet in the morning, mid-afternoon, and in the evening, if needed. The tablet should be swallowed whole to preserve the timed-release action.

Also available—for those who prefer palatable liquid medication—

Tussagesic suspension

NEW

Tussagesic

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska • Peterborough, Canada

ment for the production of nitrogen and organic chemical products. In 1950, Mathieson assisted in forming—and in 1951 acquired the shares owned by the public in—Mathieson Hydro Carbon Chemical Corporation, which started producing organic chemicals in 1952. In the same year, through a merger with E. R. Squibb & Sons, Mathieson extended its activities into the fields of drugs and pharmaceuticals, and in 1953 and 1954, through certain minor acquisitions, extended its interest in the production of basic pesticide ingredients and concentrates and the packaging of anti-freeze and other automotive specialties.

The growth of the corporation following the Olin Mathieson merger has continued into fields established by the diversified experience and interest of its two predecessors. In 1955, the corporation acquired Blockson Chemical Company of Joliet, Illinois, a producer of sodium phosphate and related by-products. This acquisition complemented the corporation's position in industrial chemicals and plant foods, and has provided a base for the expansion of the firm's chemical business in the Chicago industrial area.

Later in 1955, the Brown Paper Mill Company, Inc., and four related converting companies were acquired. Brown Paper owned an integrated pulp and paper mill, most of the output of which was processed by the converting companies into kraft paper and paperboard products. In addition to the paper mill, Brown paper owned approximately 465,000 acres of timber properties in Louisiana, Arkansas and Texas. As part of its expanding interest in aluminum fabrication, Olin Mathieson in December, 1955 acquired a manufacturer of aluminum extrusions in Gulfport, Mississippi, and in May, 1957, a fabricator of wire and cable in Chattanooga, Tennessee.

In August, 1956, Olin Mathieson and Revere Copper & Brass, Inc., organized a jointly owned company, Ormet Corporation, to construct and operate an alumina plant at Burnside, Louisiana, on the Mississippi River, with an annual capacity of 345,000 tons of alumina, and an aluminum reduction plant at Omal, Ohio, on the Ohio River, with an annual capacity of 180,000 tons of primary aluminum, which will absorb the entire production of the alumina plant. These facilities are now in partial operation, and are scheduled for completion by the end of this year.

In 1957, the company's sales were divided as follows: industrial chemicals 20.6 per cent; arms, ammunition and explosives, 15.5 per cent; phosphate chemicals and plant foods, 15.9 per cent; drugs and pharmaceuticals, 17.7 per cent; film paper and forest products, 17.6 per cent; metals, 10.7 per cent; nuclear and high energy fuels, 2 per cent.

Considering the tremendous scope of the company's operations, it is easy to charge management with excessive diversification that could tax most competent executive leadership. Compared to the rest of the chemical industry, the company's pre-tax profit margins and its return on invested capital leave much to be desired, possibly a reflection of the difficulties involved in managing a collection of unrelated industrial enterprises.

Earnings in the past five years consequently have not been impressive, despite an increase in sales from $468 million in 1953 to $593 million in 1957. Per share operating net income was $2.77 in 1953, reached a peak of

A CIBA Documentary Report

How clinicians evaluate the safety and effectiveness of RITALIN® as a psychic stimulant

CONDITIONS TREATED	RESULTS	COMMENTS ON SAFETY
Depression accompanying chronic illness and convalescence from short-term illness; mild depression induced by life pressures; overtranquilization.	"The drug gave a plateau type of stimulation, smooth onset, with no euphoria . . . The effect lasted about four hours, gave the patient a feeling of well-being . . ."	"The side effects of Ritalin are minimal." "The work showed that the drug had no effect on blood pressure, the blood count, urine or blood sugar, did not depress the appetite, and produced no tachycardia."[1]
Lethargy, fatigue and emotional depression secondary to chronic illness in elderly patients; mild depression secondary to short-term illness. (Twenty-three "normal," healthy people also received the drug.)	"For the entire 112 patients 66 per cent showed marked improvements [obvious drug effect and mood improvement] . . ."	"No serious side reactions were noted . . . In no case was it necessary to stop the drug. No evidence of significant effect upon blood pressure or pulse has been found. This is particularly interesting, since these side effects have been common with other mood elevating drugs . . ."[2]
Drug-induced psychophysiologic depression; physiologic after-effects of certain anesthetics; barbiturate intoxication; moribund states due to systemic infection. (All patients were epileptic, mentally retarded and/or brain damaged.)	"All except two [of 129] patients responded to the initial injection [of parenteral Ritalin] within 1½ to 15 minutes."	"In no instance was there any evidence of untoward effects." ". . . the very poor basic physical condition of our patients in this study, those associated with profound chronic brain damage, accentuates the safety of parenteral Ritalin . . ."[3]

DOSAGE: *Oral:* Dosage will depend upon indication and individual response. Many patients respond to 10 mg. b.i.d. or t.i.d. Others will require 20-mg. doses. In a few cases, 5-mg. doses will be adequate. If inability to sleep is encountered, last dose should be given before 6 p.m. *Parenteral:* 10 to 30 mg., intravenously or intramuscularly.

RITALIN® hydrochloride (methylphenidate hydrochloride CIBA)

2/2003MK

References: 1. Natenshon, A. L.: Dis. Nerv. System 17:392 (Dec.) 1956. 2. Landman, M. E., Preisig, R., and Perlman, M.: J. M. Soc. New Jersey 55:55 (Feb.) 1958. 3. Carter, C. H., and Maley, M. C.: Dis. Nerv. System 18:146 (April) 1957.

CIBA SUMMIT, N. J.

Olin Mathieson	
Price 40	Capitalization (3/3/58 Pro Forma)
Dividend $1	Long-term Debt $330,270,000
Yield 2.5%	Common Stock ..... 13,282,121 shs.
1958 Price Range 43½-31½	
Traded ..... N.Y.S.E.	

$3.36 a share in 1955 and then declined to $2.67 in 1957. This year, very large write-offs of pre-operating expenses, connected particularly with the aluminum program, as well as the effects of the recession have combined to reduce earnings to only 74¢ a share for the first half of 1958, down from $1.48 a share in the same period of last year. Moreover, in the third quarter of 1958, about 75¢ per share after taxes of deferred pre-operating expenses accumulated in the past several years will be written off. Thus earnings for the full year 1958 will be reported at a level far below the average of slightly under $3.00 per share earned in the past five years.

However, now that the bulk—if not all—of the bad news is behind the company, a number of rays of hope begin to emerge. The management organization has recently been strengthened in various ways. With the recovery from the recession now well underway, sales should improve, particularly sales of industrial chemicals, forest products and metals. The Squibb drug division continues profitable, and is far advanced in cancer research. Farm chemicals, with a decent break in weather conditions, should improve somewhat next year. Boron-based high energy fuels, although unprofitable now, do have considerable promise looking five to ten years ahead.

This is not to say that all the company's problems are being solved rapidly. The major immediate headache is developing enough demand for Olin aluminum to allow the company to break even on its very costly new facilities. The company is not likely to break even on its aluminum operations till 1959 and substantial profits are unlikely before late 1960 or 1961. Aluminum continues in oversupply, competition is very keen, and growth of demand in the past few years has been somewhat below expectations.

Against this background, let us try to evaluate the common stock making several assumptions. Assuming that economic conditions over the next two or three years will be such as to enable the company again to earn the $3 per share which it averaged in the 1953-57 period; assuming that the aluminum venture will pass its break-even point and begin to be profitable in the early 1960's; and assuming that the company's return on invested capital is restored to its pre-major expansion rates, even though these rates are somewhat below average for the industry, earnings of $4 or $5 a share can be projected assuming full conversion of outstanding debt.

Applying to these earnings the average price-earnings ratios of a high of 20 and a low of 15 which prevailed between 1954 and 1957, substantial opportunities for eventual capital gains can be visualized. Of course, considering the spotty past record of the company, the shares are recommended only for patient investors who can afford speculative risks. For the more conservative investor, the two convertible debenture issues have attraction for moderate, longer-term appreciation possibilities and higher current income.◀

Natalins *(Mead Johnson)*

Prenatal vitamin and mineral tablets in two formulations: *Comprehensive* supplies 12 vitamins and minerals, *Basic* supplies four basic vitamins and minerals. *Indications:* As a dietary supplement during pregnancy and lactation. Particularly useful for protection of multiparas. *Dosage:* One tablet daily, or as indicated. *Supplied:* Either formulation in bottles containing 100 tablets.

Tussagesic Tablets and Suspension *(Dorsey)*

Each timed-release tablet contains 50 mg. of *Triaminic,* 30 mg. of *Dormethan,* 180 mg. of terpin hydrate, and 325 mg. of N-acetyl-para-aminophenol. Each teaspoonful of suspension contains 25 mg. of *Triaminic,* 15 mg. of *Dormethan,* 90 mg. of terpin hydrate and 120 mg. of N-acetyl-para-aminophenol. *Indications:* For comprehensive control of all cold symptoms, decongestion of nasal and paranasal membranes, elimination of irritating secretions. Provides relief from rhinitis, rhinorrhea, lacrimation and sneezing, control of the cough reflex. *Dosage:* As directed by the physician. *Supplied:* Tablets, in bottles of 50. Suspension, in bottles containing 1 pint.

Duadacin *(Lloyd)*

Each capsule contains 5 mg. of phenylephrine hydrochloride, 1 mg. of chlorpheniramine maleate, 12.5 mg. of pyrilamine maleate, 30 mg. of caffeine, 50 mg. of ascorbic acid, 130 mg. of acetophenetidin and 200 mg. of salicylamide. *Indications:* For relief of cold symptoms. *Dosage:* Adults, one capsule three or four times daily. *Supplied:* In bottles of 100 capsules.

Dimetane Ten Injectable
Dimetane 100 Injectable *(Robins)*

Two parenteral dosage forms of the antihistaminic, parabromdylamine maleate. *Dimetane Ten* contains 10 mg. of the drug per cc., *Dimetane 100* contains 100 mg. per cc. *Indications:* For symptomatic relief of many manifestations of the allergic state, such as hyposensitization reactions, reactions to drugs and blood transfusions, urticaria, allergic rhinitis and many pruritic dermatoses. Particularly indicated where rapid response is desired, and for those patients in whom oral therapy may be impractical. Effect is usually obtained within 15 minutes and may persist for 12 hours. *Dosage:* As directed by the physician. *Supplied: Dimetane Ten,* 1 cc. ampuls in boxes of six. *Dimetane 100,* 2 cc. multiple dose vials in boxes of one.

V-Cillin K, Pediatric *(Lilly)*

Each 5 cc. teaspoonful contains 125 mg. of penicillin V potassium. Readily soluble form, oral solution. *Indications:* In the treatment of all infections caused by penicillin-sensitive organisms. May be given in place of injectable penicillin in treating most infections. *Dosage:* Usual pediatric dose in mild and moderately severe infections is 125 mg. every 4 to 6 hours. In severe infections, 250 mg. may be given every 6 hours. *Supplied:* In bottles containing 40 and 80 cc.

Neobiotic Tablets *(Pfizer)*

Oral bowel sterilizer. Each tablet contains 500 mg. of neomycin sulfate equivalent to 350 mg. of neomycin base. *Indications:* For suppression of the usual bacterial inhabitants of the colon as a prophylactic measure in surgery of the large bowel and anus. Active against a variety of aerobic bacteria including staphylococci, pseudomonas and proteus. *Dosage:* Suggested dose is 1 gm. (2 tablets) every four hours for 24 to 72 hours prior to surgery. *Supplied:* In bottles of 20 and 100 tablets.

Desoxyn Gradumets *(Abbott)*

New product form. Long-acting oral dosage, central nervous system stimulant. *Indications:* In the management of obesity, depressed psychopathic states, and in the management of mental depression accompanying illness, convalescence, old age or menopause. In the management of narcolepsy with or without cataplexy. A useful adjunct in the management of Parkinsonism. *Dosage:* As directed by the physician. *Supplied:* Gradumets in 5 mg., 10 mg. or 15 mg. strength in bottles of 50 and 500.

Protef Rectal Suppositories *(Upjohn)*

Each suppository contains 15 mg. of hydrocortisone acetate and 15 mg. of neomycin sulfate (equivalent to 10.5 mg. of neomycin base). *Indications:* Anal fissure, postoperative edema, radiation proctitis, cryptitis, papillitis, nonspecific localized proctitis, anusitis, mechanical trauma, irritation, postoperative treatment of fistulectomy, hemorrhoidectomy. *Dosage:* One suppository moistened with water and inserted gently may be repeated two to four times daily. *Cautions:* Should be used with caution in patients already receiving corticosteroid therapy orally or parenterally, as 20 to 40 per cent of rectally administered hydrocortisone may be absorbed. Use should not be continued for longer than four to seven days. *Supplied:* Packages of 12 foil-wrapped suppositories.

Cosa-Tetracyn Pediatric Drops *(Pfizer)*

Glucosamine-potentiated tetracycline hydrochloride in pediatric dosage form. *Indications:* For infections caused by Gram-positive and Gram-negative bacteria, rickettsiae, certain spirochetes, large viruses and protozoa. Provides increased absorption of tetracycline, yielding higher blood levels and helping to minimize gastrointestinal disturbances. *Dosage:* Average daily dose for infants and children is 10 to 20 mg. per lb. of body weight in divided doses at 6 hour intervals. *Supplied:* In 10 cc. bottles containing 1.0 gm. of tetracycline for reconstitution. When reconstituted the suspension contains 100 mg. of glucosamine-potentiated tetracycline activity per cc.

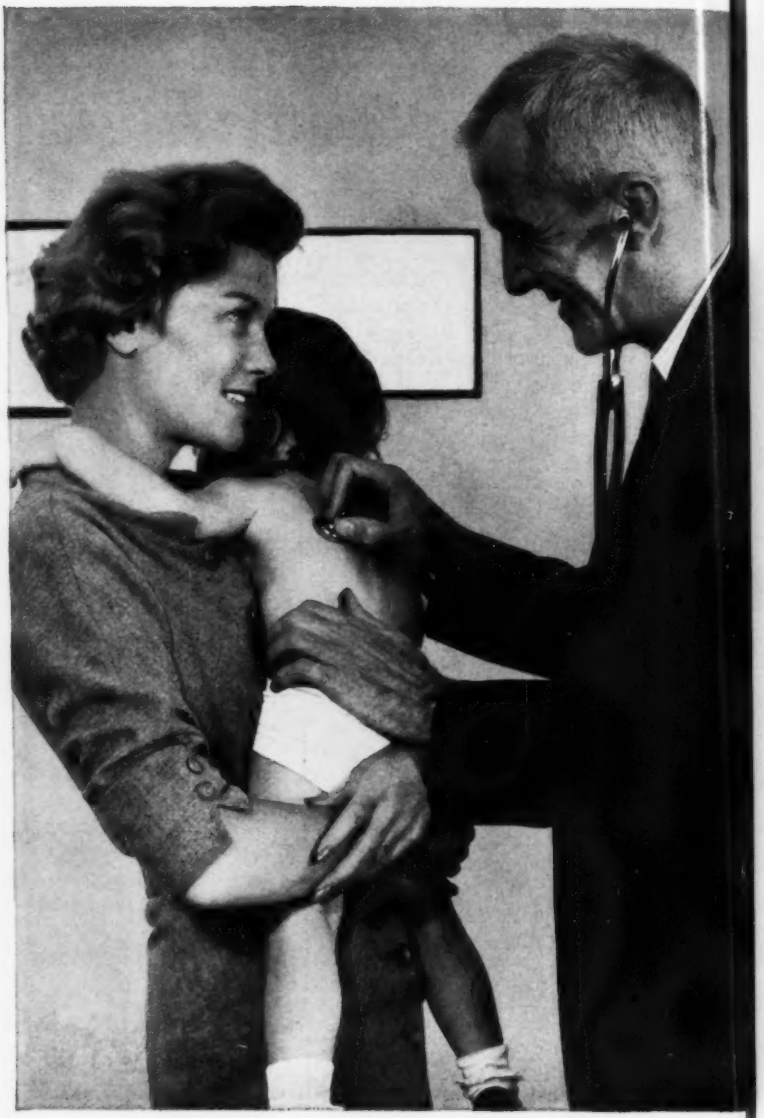
Compocillin-VK *(Abbott)*

Potassium penicillin V granules for oral solution. Reconstituted with water they make a solution for oral administration with higher, faster blood levels than those attained with equivalent amounts of penicillin V acid or potassium penicillin G. *Indications:* For all infections amenable to oral penicillin therapy and as a prophylactic agent against recurrence of rheumatic fever, in the management of rheumatic carditis, and in preventing secondary bacterial infection. It may also counteract complications in severe viral attacks. *Dosage:* As determined by the physician. *Supplied:* 1 gm. in 40 cc. containers and 2 gm. in 80 cc. containers. Addition of 24 cc. of water to 1 gm. or 48 cc. of water to 2 gm. makes a solution containing 125 mg. in each 5 cc. teaspoonful.

Di-Isopacin *(Con. Midland)*

Each tablet contains a balanced combination of 0.75 gm. of sodium para-aminosalicylate and 25 mg. of isoniazid. *Indications:* For use in patients with active tuberculosis due to streptomycin-resistant organisms, or who are not responding to streptomycin therapy, and in order to delay emergence of resistant strains. The drug is considered an adjunct to recognized therapeutic measures, such as rest, nutrition, surgical measures, etc. *Dosage:* 2 to 4 mg./Kg. of body weight of isoniazid content. The usual adult dose is 8 to 12 tablets daily in divided doses. *Precautions:* Indiscriminate use of isoniazid should be avoided since it may lead to a loss in efficacy at a time when the drug may be needed for emergency use. *Supplied:* Bottles of 500 and 1000 tablets.

"Much better



Effect of Competitive Industrial Activity on Severely Disabled Cardiac Patients

Physical demand of work exceeding the physical capacity of the cardiac patient was listed by 71 per cent of the industrial physicians surveyed, as a major reason for reluctance in hiring these persons. Next came the risk of loss arising out of compensation claims (42%), the heavy burden on company-sponsored insurance programs (30%), insufficient medical staff (12%), and policy of personnel department (11%). Only eight per cent of these physicians considered cardiac patients to be unsafe workers, and only three per cent considered them to be inefficient.

Eight of 19 industries stated that during the past year 242 persons known to have cardiac vascular disease were among the total of 19,321 new workers employed. Asymptomatic hypertension was the most common diagnosis, followed in order by rheumatic heart disease, heart disease type undertermined, and arteriosclerotic heart disease. Only 24 new employees had been given a diagnosis of arteriosclerotic heart disease, despite the frequency of this disease in the adult male population of the United States. All 19 industries reported that it was their policy to return an employee to his job after recovery from an acute heart attack.

A report on 19 employees all classified as having severe or advanced heart disease may be considered unique. Excellent attendance records, and not one reported case of compensable injury, are contrary to the stated reasons given by industry for not employing cardiac patients. The absence of any detrimental effect of employment on the disease state is well documented in the literature. The remarkable improvement exhibited by some of the employees makes one wonder whether the dictum that the person with severe cardiac disease requires constant rest and should retire from employment should not be revised for employment in a compatible job can, in the specific case, be beneficial.

Slipyan, A., *J.A.M.A.*, 168:147-153,1958.

Arctic Anemia

Anemia occurred unexpectedly in six men of an expedition conducting a scientific exploration of the central Greenland Ice Cap, as revealed by weekly measurements of hemoglobin and red cells in the peripheral blood of each over a period of 3½ months. All were at hard physical exercise, low temperatures, moderately high altitudes and in continuous daylight.

Unaccountably, the red-cell count fell faster than the hemoglobin. The possibility that the "anemia" was merely a change in plasma volume without change in the erythrocytes

after cold exposure must be considered. It may be surmised that it is possible for bleeding to occur without obvious hemorrhage, and extravasation of blood may result from severe muscular exertion. Muscular exercise in dogs has been known to produce anemia. Strenuous exercise in athletes may lead to a fall in the level of red blood cells.

Observers of miners with silicosis, living at high altitudes, note that when arterial oxygen saturation was from 60 to 70 per cent of normal a decrease in hemoglobin levels and total red-cell counts occurred. It is suggested that there are limits between which the marrow responds when oxygen tension varies, and that polycythemia is not the only possible blood response to decreased oxygen tensions at high altitude. Cold may also be involved in this problem.

Christie, R. W., *New England J. Med.*, 259:605-611, 1958.

Bleeding Duodenal Ulcer

In hemorrhagic duodenal ulcer the mucosal capillaries are gravely injured, as indicated by histopathologic findings. The inflammation of duodenal mucosa is associated with its capillary dysfunction. Mucosal lesions are a pathologic development of a localized capillary syndrome. Since water-soluble citrus bio-flavonoids exert an anti-inflammatory effect and restore capillary integrity, 36 patients with hemorrhagic duodenal ulcer were treated with a milk-orange juice-gelatine mixture and a modified Meulengracht diet supplemented with *C.V.P.*, a bio-flavonoid compound. All 36 patients responded to the combined treatment. Bleeding was arrested and the stool was free of blood in from six to eight days, except in two cases where traces of blood were found in the stool for 10 and 13 days respectively. X-rays revealed that the mu-

cous membrane and the duodenal contour returned to normal after 10 to 20 days.

Weiss, S., et al., *Am. J. Gastroenterology*, 29:629-642,1958.

Carcinoma of the Lung

The simultaneous occurrence of tuberculosis and bronchogenic carcinoma should be suspected in all patients with pulmonary tuberculosis who show an enlarging focus, develop an obstructing infiltration, or have a cavity with few demonstrable tubercle bacilli. In 228 proved cases of bronchogenic cancer the average duration of symptoms from onset to positive diagnosis was 7.6 months. Signs of endobronchial obstruction were the most common physical signs; 97 per cent of patients were suspected by the roentgenologist to have the disease. Cancer cells were noted in 47 per cent of 61 patients whose bronchial aspirates were examined after bronchial lavage. Forceps biopsy was positive in 25 per cent.

It was observed that a majority of men over 40 who smoke cigarets smoke at least a package a day, whereas only a small minority of women over 40 who smoke cigarets consume this many. In a detailed study on the death rate among physicians in England from lung cancer, it is stated that the death rate per year rose from 0.07 per 1,000 in nonsmokers to 1.66 per 1,000 in heavy smokers—the death rate of heavy smokers from lung cancer was 20 times greater than that for nonsmokers. There was a progressive and significant reduction in mortality with the increase in length of time over which smoking had been given up.

At least 24 months elapsed in most cases between the first roentgen evidence until operation or death.

Seley, G. P., *New York J. Med.*, 58:2967-2972,1958.

Ex-Smokers

Questionnaires on smoking habit were mailed to a sample of 5,99: men selected from telephone direc tories from all parts of the Unitec States. A second letter was sent tc those who failed to reply to the first A total of 3,705 questionnaires were returned of which 3,560 were satisfactory for analysis.

Of 3,560 men who filled out a questionnaire on smoking habits, 2,498 (70.2 per cent) stated that they smoked cigarets regularly or had done so in the past. Of these 2,498 men, 472 (18.9 per cent) stated that they no longer smoked cigarets or tobacco in any form. A questionnaire asking why they had stopped smoking and the effects, if any, of giving up smoking was sent to the 472 ex-smokers, and 333 (70.6 per cent) replied.

Only 6.3 per cent of the 333 ex-smokers said that they gave up the habit because of reports linking smoking to lung cancer and an additional 2.4 per cent said that they gave it up because of reports that smoking has a bad effect on health in general. Only 1.6 per cent of men with a history of regular cigaret smoking said that they gave up the habit because of reports relating cigaret smoking to lung cancer or other diseases. Some condition apparently made worse by smoking—coughing most frequently —was given as a reason for stopping by 208 (62.5 per cent) of the 333 ex-smokers.

Some improvement, such as less coughing, less shortness of breath, etc. was noticed noted by 272 of the men as an apparent result of giving up smoking. Of the ex-smokers 246 (73.9 per cent) said that they gained weight when they stopped smoking.

Hammond, E. C., & Percy, C., *New York J. Med.*, 58:2056-2059,1958.

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Protection Against Tetanus

Present evidence indicates that immunization with tetanus toxoid produces continuous protective serum levels of antitoxin in all people for five years and in most people for 10 years. It would appear that booster doses of tetanus toxoid every five years would produce serum antitoxin levels which are continuously protective against tetanus. This continuous protection will aid in the prevention of tetanus due to trivial untreated wounds. A booster dose of tetanus toxoid apparently will elicit a protective antitoxin level in people 10 and possibly more years after their last booster dose, regardless of how low their levels are previous to stimulation. A booster dose should be given to all immunized people who are exposed to tetanus if it has been over one year since their last dose of toxoid. The use of both tetanus antitoxin and tetanus toxoid is indicated in certain clinical situations. They may be used concomitantly if they are injected into different extremities and if separate syringes are used.

Physician's Bull., 23:188-190,1958.

Pulmonary Thromboembolism

Recent work has cast much doubt on the value of ligation of the superficial femoral or common femoral veins in the prevention and/or treatment of pulmonary embolism. Evidence supports the value of anticoagulant therapy in its prevention and treatment. It is a disease of the aged, especially the patient with cardiac or metastatic malignant disease, or one who has undergone laparotomy or lower-extremity amputation. The source of the majority of pulmonary emboli is asymptomatic leg vein thrombosis. When pulmonary embolism is considered, a leucocyte count, multiple-lead electrocardiogram, and possibly a serum bilirubin test should be made immediately. Within 48 hours a chest x-ray should be done. If the diagnosis is in doubt, and if no contraindications to the use of anticoagulants exist, the patient should be given anticoagulant therapy. Prophylactic anticoagulation also appears to have great promise in lowering the incidence and fatality.

Hanway, J. W., *New York J. Med.*, 58:2783-2788, 1958.

Rare Development in Pulmonary Heart Disease

The syndrome of carbon dioxide narcosis is precipitated by oxygen administration in a small percentage of patients with a high carbon dioxide content of the blood. Death from anoxia in patients with chronic pulmonary disease is much more common than is death from CO_2 narcosis. Oxygen should be administered to patients with CO_2 retention with great care and the patients observed as carefully as are those in diabetic coma in order to prevent CO_2 narcosis.

Utilization of the Drinker respirator and Bennett valve and performance of tracheotomy are all directed toward making the inhaled oxygen more readily available. Tracheotomy decreases the dead space by as much as 50 per cent and so is an invaluable procedure in cases of severe anoxia. The operation makes it much easier to keep the trachea free of secretions. The Drinker respirator has two disadvantages:

1. Difficulty in nursing care.
2. Possibility of negative inspiratory pressure producing pulmonary edema.

If the patient breathes voluntarily use of the Bennett valve tends to obviate the objections to the use of the Drinker respirator and allows the efficient administration of bronchodilators under pressure.

Almost all these patients have an element of infection and the use of antibiotics plays an important role.

Leight, L., *J. Kentucky M.A.*, 56:880-881,1958.

Indications for Parenteral Iron

Hypochromic anemia should be treated by injections when one or more of the following considerations apply:

1. Malabsorption of iron, which may be associated with total or subtotal gastrectomy, intestinal disease, steatorrhea, reduced intestinal absorptive surface or very rarely unexplained.
2. Inability to be sure that oral medication is taken, as sometimes is the case with inmates of institutions, occasionally in children, and when unfavorable environmental factors create uncertainty.
3. Refusal to take iron by mouth.
4. For a rapid therapeutic effect, as in the case of hospitalized patients with severe hypochromic anemia whose calculated degree of iron depletion may be completely corrected by daily injections.

Severe systemic reactions including convulsions have followed the intravenous administration of saccharated iron oxide and have been attributed to instability on prolonged storage. Consequently this product has been largely replaced in the therapy of iron deficiency anemia by a recently developed intramuscular preparation, *Imferon*, which is well tolerated and effective.

Bethel, F. H., *GP*, 18:97,1958.

Lung Cancer Death Rates in England and Wales Compared with Those in the U.S.A.

The lung cancer death rate reported by the Registrar General for England and Wales in 1955 was 69.3 per 100,000 population for males, 10.6 per 100,000 for females. Standardizing the lung cancer death rates reported by the National Office of Vital Statistics for the United States in 1955 to the age distribution of the population of England and Wales in 1955, the rates were 33.0 per 100,000 population for males, 6.7 per 100,000 for females. In other words, the lung cancer death rate in England and Wales for males was 2.1 times as high as in the United States, and for females 1.6 times as high. These ratios did not vary greatly in different age groups.

There is evidence that in both countries lung cancer is highly associated with cigarette smoking. At least five different factors may be of importance in determining the degree to which the lungs of a cigarette smoker are exposed to important ingredients of the smoke:

1. The average number of cigarettes smoked per day.
2. The number of years of smoking.
3. The degree to which the smoke is inhaled.
4. The proportion of each cigarette which is actually smoked.
5. The amounts of various chemical ingredients in the main smoke stream of the cigarette.

Among both males and females in the middle and old age groups there are proportionately more cigarette smokers in the United Kingdom than in the United States, but the number of cigarettes consumed per smoker per day is higher in the United States.

Cigarette butts discarded by several different groups of people in the Netherlands were collected and measured. The mean length was 19.7 mm. —19.6 per cent less than 15 mm., 55.6 per cent less than 20 mm. These are preliminary figures. Nevertheless, the very large difference between the findings in the Netherlands and in the United States is suggestive. If an equally large difference of this kind exists between the United Kingdom and the United States, it may well account for the difference in reported lung cancer death rates.

In the United States the average length of the butt discarded is 31 mm.; five per cent are 45 mm. or longer, nine per cent are under 20 mm. In the United States in 1957 the main smoke stream of the average cigarette contained 2.6 mg. of nicotine and 42.8 mg. of tar. More recently, cigarettes lower in nicotine and tar have become increasingly popular in the United States.

In both countries the lung cancer death rate of smokers as well as of nonsmokers is higher in urban than in rural areas, far greater between Liverpool and rural areas of Wales than between large cities and rural areas in the United States. However, Merseyside (which includes Liverpool) has a higher male lung cancer death rate than any other region in England and Wales, so it cannot be considered as typical of the country as a whole.

The reported death rate from cancer, exclusive of lung cancer, declined steadily from 1931-5 to 1956 in England and Wales, but rose slightly in the United States during the same period of time. It is possible that differences in the diagnosis and recording of causes of death may account for a part of the difference between reported lung cancer death rates in the two countries.

Hammond, E. C., *Brit. M.J.*, 2:649-654,1958.

briefs: SURGICAL

Vagotomy for Bleeding Duodenal Ulcer

Sixty patients who had had one or more episodes of massive bleeding from proved duodenal ulcer were treated by means of vagotomy and a drainage procedure. Pyloroplasty was employed 55 times and gastroenterostomy five times. There was one surgical death, four other failures, two of which had recurrent bleeding. Two patients who had obtained good results died of unrelated causes. One patient was untraced. Fifty-two of 57 treated and traced cases obtained satisfactory results (91.2%). The entire group had an average follow-up of 3.7 years.

The higher reported mortality rates when these cases are treated medically or by gastrectomy are due in large measure to delay in surgery. This reluctance, on the part of patient and physician alike, will only be overcome by demonstration of a more satisfactory method of treatment. In vagotomy and pyloroplasty there may be such a method.

Dorton, H. E., *J. Kentucky M.A.*, 56:855-861,1958.

Complicated Diverticulitis

The morbidity associated with the surgical treatment of diverticulitis remains high. Some complication has developed in 30 per cent of such patients in the form of obstruction or perforation of the colon, a fistula between the colon and bladder, or the colon and vagina. Complications may develop without warning and often perforation, fistula formation or obstruction occurs before the diagnosis is made.

Twenty-five per cent of the patients studied were under 50 years of age. These patients are much more likely to require surgical intervention than older patients with diverticulitis. In 57.2 per cent, symptoms had been manifested for over a year.

Nearly all the patients operated on had severe diverticulitis and some complication. This was true for many of the 69 patients in whom a one-stage resection of the diseased colon was carried out. Partial obstruction was frequent, and small abscesses were found between the colon and bladder or between the colon and the lateral abdominal wall in many cases. Some patients with a small colovesical fistula were submitted to a one-stage resection and primary anastomosis. No deaths occurred in this group, indicating that in diverticulitis without obstruction or extensive inflammatory reaction surrounding the involved colon, a one-stage resection may be carried out with little risk. The average hospital stay for all after one-stage resection was 15 days—60 days for patients who required a three-stage resection.

In the past 10 years, 131 patients were operated on for diverticulitis

with a mortality of 1.5 per cent (2 deaths). Sixty-nine (52.6 per cent) had a one-stage resection with a primary anastomosis. No deaths occurred in this group. Forty (30.5 per cent) had previously undergone one or more operative procedures that did not relieve symptoms or led to further complications. Thus, inadequate surgery is one factor responsible for many of the complications incident to the surgical treatment of diverticulitis.

Further reduction in the morbidity of this disease must come from earlier operation. Resection of the diseased bowel stops the recurrent attacks; perforation, obstruction and fistula formation are prevented, and the danger of allowing unsuspected carcinoma to go untreated is eliminated.

Colcock, B. P., *New England J. Med.*, 259:570-573, 1958.

The Surgical Treatment of Chronic Ear Disease

The fenestration operation is done for otosclerosis where the stapes is fixed and the oval window immobile. The fenestra (window) is made in the lateral semicircular canal where it enters the vestibule, and is covered with a flap attached to the ear drum. The hearing can never be brought up to true normal.

Stapes mobilization frees the immobile stapes so that it can vibrate. The ossicular chain returns more or less to its functioning aspect. Some patients' hearing can be brought back to normal.

There seems to be a great increase in chronic tympanic effusions—possibly a by-product of the use of antibiotics. If untreated this results in an adhesive, suppurative process with persistence of tympanic perforations and ossicular chain necrosis, causing increasing conduction deafness.

Tympanoplasty is a reconstruction of the middle ear as an air-containing cavity and of some part of the ossicular chain so as to permit air-conducted sound vibrations to pass through the oval window. It is not always possible to say how much of the ossicular chain is destroyed, the condition of the two windows, or the extent of the pathological process elsewhere. Removal of all pathological changes can only be done after the suppurative process has been brought under complete control.

Myringoplasty is repair of central perforations by full or three-quarter thickness skin grafts. Many of these perforations can be made to close by office treatment.

There are inherent difficulties in most tympanoplasties. A free graft is not certain to "take." Recently the middle ear was reconstructed with a pedicle flap from the temporal muscle and then a fenestration was done. Only a few cases have been done, but excellent results were obtained. In a patient on whom this operation was performed there has been a 10 to 15 decibel increase in hearing throughout all frequencies at the end of three months, indicating that the principle may be correct.

MacCready, P. B., *Connecticut M.J.*, 22:531-536, 1958.

briefs: GYNECOLOGIC

Treatment of Trichomoniasis

Trichomoniasis is a contagious disease caused by microscopic protozoa, that often infects the vaginal tract despite efforts to insure personal hygiene. This disease affects nearly 20 per cent of the female population in the United States. Of 58 patients suffering from intense itching, inflammation and malodorous discharge resulting from this infection, successful results were obtained in over 93 per cent following the use of *Vagisec* therapy. Negative cultures were obtained in three consecutive months after completion of therapy. The therapy provides a three-way surface action and contains a chelating agent, a wetting agent and a detergent.

Giorlando, S. W., & Brandt, M. L., *Am. J. Obst. & Gynec.*, 76:666-669,1958.

Uterine Curettage

No curettage is complete until an ovum forceps or a kidney stone forceps is inserted, opened and closed, in an attempt to grasp a polyp that may have been missed. In every curettage, unless there is strong contraindication, multiple biopsies of the cervix should be taken at the squamocolumnar junction. The curettings should be collected in a continuously irrigated pool of 2% sodium citrate contained within the vaginal cavity and the enmeshing of tissue by the coagulum, strained through fine-mesh gauze and washed in citrate or saline solution. Cold water washing is adequate if done quickly and the tissue immediately placed in a fixative solution—one to two ounces of 10% formalin—and the tissue left for 12 to 24 hours before sectioning.

Hyperplasia of the endometrium, a common cause of functional uterine bleeding, is a result of either endogenous or exogenous hyperestrinism. If the estrogen level is kept high, bleeding will not occur; if there is a lowering of the estrogen level, deprivation bleeding will ensue. Estrogens used in the treatment of the menopause syndrome often cause irregular bleeding and so make the diagnosis difficult. Hyperplasia of the endometrium occurs frequently at puberty and during the premenopausal and postmenopausal epochs. In the postmenopausal phase it is a precancerous lesion. Curettage is often indicated to establish the diagnosis and to arrest the bleeding.

In a study of the problem of infertility, a curettage gives valuable information. In functional uterine bleeding a curettage is often curative; in many cases there is spontaneous subsidence of bleeding. Intractable spasmodic dysmenorrhea will at times respond to a thorough dilation of the cervix. The insertion of a stem pessary in the cervix may give relief. Curettage should be done in all cases of noninfected incomplete abortion.

Tissue serves as a medium for the growth of bacteria and as a potential source of hemorrhage and should be removed with sponge or ovum forceps and a wide-spectrum antibiotic given parenterally in large doses immediately before and after curettage.

Hobbs, J. E., *Mississippi Valley M.J.*, 80:116-119, 1958.

Treatment of Trichomonas Vaginalis

Tritheon, an Italian preparation, was administered to two groups of patients with this form of vaginitis. Group 1 was treated orally, group 2 with a combined topical and oral use of the drug. The 23 in group 1 had the drug in daily dosage of 300 mg. for 8 days, and were reexamined for T. vaginalis 3 times. At the first examination 13 were found clinically cured. A second course completely relieved an additional 6. Spermatic fluid from 11 of the husbands showed 6 were infected with T. vaginalis. These were given Tritheon, 300 mg. daily for 20 days. The treatment was effective in 5. Better results were had from the combined therapy given to the 25 women in group 2. These had daily doses of 800 mg.—300 mg. orally, 500 mg. topically. The first course effected complete remission of symptoms in 18, the second course achieved complete remission in 5 of the remaining 7. The drug was well tolerated and is recommended for prolonged use. *(Original in Italian.)*

Bertoli, P. E., *Minerva ginec.*, 9:1006-1010,1957.

briefs: PEDIATRIC

Peculiarities of Symptomatology in Chronic Poliomyelitis Patients

The development and improvement of tank-type respirators, cuirass respirators, rocking beds, and "positive-pressure" devices during the past two decades have made possible greatly improved medical care for victims of respiratory paralysis. These patients are particularly subject to pyelitis, pyelonephritis, ureteral obstruction due to calculi, pneumonia, lung abscess, and phlebitis. There are now some 1100 such patients at home under the care of their physicians and 550 more will soon be returning to their homes.

The chronic poliomyelitis patient may feel no pain in a disease in which it is ordinarily a major manifestation. Large calculi have traversed the length of a ureter without causing discomfort. Partial or complete ureteral obstruction due to a stone has occurred without renal colic. Several such patients with both viral and bacterial infections who had no fever, one of these had pneumococcal pneumonia, which nearly invariably produces fever in other persons. Many patients are afebrile who have pyelitis and obstructive uropathy due to various organisms. The same is true of pharyngitis and bronchitis due to streptococci, staphylococci and other bacteria. Peritonitis due to *A. aerogenes* was observed to occur without fever in one case. As with the absence of pain, lack of fever occurs only in the very severely affected patients. Poliomyelitis patients usually have a temperature of 97.4° to 98° orally. Temperatures over 102 are encountered infrequently and those lower than 100 may represent fever.

Although these patients may have no fever or localizing pain with various intercurrent diseases, there is usually some "displaced" complaint which may be the only indication that all is not well. Gastrointestinal complaints frequently are made with non-alimentary disease processes, *e.g.*, vague abdominal discomfort and/or distention in partial or complete ureteral obstruction, hypoxia, and, in one patient, with peritonitis. These symptoms are due to adynamic ileus, gastric dilation or both. Because of its relationship with emotional states, gastric dilation is by far the most common gastrointestinal abnormality.

Intercurrent disease in chronic poliomyelitis patients may go unnoticed or evade detection because of failure of the body economy to respond to the illness in the usual manner. The high incidence of calculi of the urinary tract with lack of pain requires excretory urograms whenever gastric dilation, ileus or vague abdominal complaints are presented. Abdominal paracentesis may diagnose peritonitis without fever and leukocytosis. Subjective feelings of lack of air may be

the only indication of pneumonia or atelectasis; gastric dilation or anxiety may cause the same symptoms. It is suggested that such patients should be hospitalized promptly if the cause of intercurrent illnesses is not immediately evident.

Sweet, A. Y., *J. Mt. Sinai Hosp.*, 25:405-410,1958.

A Case of Tetanus Recovery

A white boy of 8 was hospitalized because of stiffness of the body and difficulty in opening his mouth. Ten days previously he had cut his right great toe on a garden hoe. The wound had been washed with water, then sutured. Penicillin and tetanus toxid were administered. During the next eight days the boy appeared well. Two days prior to admission, he complained of a sore throat and difficulty in swallowing. The next day cramping periumbilical pain was added. On the day of admission "drawing" of all four extremities was noted. No prior tetanus immunization had been given.

The boy was apprehensive, but oriented and cooperative. Tachycardia and tachypnea were noted. On the right great toe was a ½ inch crusted, indurated lesion. Severe nuchal-spinal rigidity was evident. The legs were held in extension, the feet in plantar flexion. The jaws could be separated only with manual assistance. The abdominal muscles were tense. The superficial and deep tendon reflexes were intact and equal, the knee jerks exaggerated the extensor spasm. During the examination periodic bouts of extreme extensor rigidity occurred, mainly in the lower extremities, back and neck.

Shortly after admission, in the operating room under general anesthesia treatment was given as follows: A tracheostomy, debridement of the wound, infiltration of tetanus antitoxin in the wound area, parenteral administration of 80,000 units of tetanus antitoxin, insertion of a nasogastric feeding tube, parenteral administration of aqueous crystalline penicillin.

Clostridium tetani was cultured from the debrided material.

During the next 20 days the calorie and fluid needs and indicated oral medications were given through the feeding tube. A total of 2.4 million units of oral penicillin V were given daily. Heavy sedation was maintained with chloral hydrate and supplementary doses of phenobarbital. Special duty nursing was provided around the clock.

Hypothermia was introduced on the third day in order to lower the metabolic rate and reduce the oxygen requirement. Intermittent generalized tonic extensor contractions, although lessening, continued during the three weeks in the hospital.

After the twenty-first day sedation was gradually withdrawn, allowing short periods of consciousness. On the twenty-fourth day the nasogastric tube was removed. The trachoestomy tube was gradually decreased in size and then removed. After x-ray examination of the vertebrae, a program of physical rehabilitation was started during the week before discharge, on the thirty-third day, with arrangements for outpatient care through convalescence and rehabilitation. At discharge, gait, speech, and coarse movements were well performed although there was general mild stiffness. Immunization with tetanus toxoid was accomplished during the convalescent period.

Adams, W. C., et al., *J. Kentucky M.A.*, 56:572-574, 1958.

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Cholecystitis with Cholelithiasis in Childhood

A four year old boy had abdominal pain, fever, nausea and vomiting for three days. His skin and sclerae had a slight icteric tinge, the urine contained a trace of bile, and the stools were acholic. The boy was hospitalized for seven days and discharged with a diagnosis of viral hepatitis.

About a year later the family physician saw the patient in his home for what he thought was an atypical appendicitis. Three days later, the mother observed an icteric tinge of the sclerae, dark urine, and lighter stools. The vague abdominal distress continued and the patient was admitted to the hospital. Examination was negative except for tenderness of the right upper quadrant. An x-ray diagnosis of chronic cholecystitis with stones was made. At operation the gallbladder had a pinkish-tan, smooth, shiny appearance, a moderately thickened wall, and contained many yellow faceted stones.

The hereditary predisposition to gallstone formation in the case is striking. The father, 35, had jaundice at 13; at operation over 100 small gallstones were removed. His only sister required a cholecystectomy at 23; their mother had the operation at 28; three of her sisters and a brother had cholecystectomies for stones before age 30. The maternal great-grandmother had a cholecystectomy and the paternal great-grandfather died at the age of 50 with jaundice.

Cholecystitis in childhood is not as uncommon as formerly believed. In considering a child with hepatitis, jaundice, or recurrent abdominal pain of obscure origin one should think of the possibility of cholecystitis and cholelithiasis.

Schwei, G. P., *Wisconsin M.J.*, 57:295-298,1958.

briefs: THERAPEUTIC

Enhancement of Tetracycline Blood Levels

Four tetracycline preparations have recently been made available, each allegedly providing higher blood levels when compared with similar doses of tetracycline hydrochloride. In the first comparisons no significant difference in plasma levels or total antibacterial activity could be demonstrated for single doses of four capsules (1 gm.) of tetracycline hydrochloride, or tetracycline phosphate complex given to the same normal subjects before breakfast, or in the plasma levels nine and 24 hours after similar doses given to the same patients in the midmorning.

In the second group an apparent enhancement of antibacterial activity of plasma was produced by two capsules of each of three tetracycline products as compared with tetracycline hydrochloride. Tetracycline base combined with sodium hexametaphosphate appeared to produce the greatest enhancement; tetracycline phosphate complex and tetracycline base combined with monobasic sodium phosphate gave similar but somewhat less enhancement. None of the differences was statistically significant, and the validity of the comparisons was further vitiated by the fact that the capsules of tetracycline hydrochloride and of tetracycline phosphate complex both also contained substantial amounts of dibasic calcium phosphate, which has been shown to depress absorption of tetracyclines.

A third comparison was made of levels of tetracycline activity in serum after ingestion of two capsules of each of four tetracycline preparations that did not contain calcium. In this study, when adjustments were made for the amounts of active tetracycline in the various capsules, each of three preparations — tetracycline hydrochloride with an equal amount of citric acid, tetracycline hydrochloride with an equal amount of glucosamine hydrochloride and a tetracycline phosphate complex—appeared to produce higher levels and total antibacterial activity in serum than the same amount of tetracycline hydrochloride. The greatest enhancement in serum activity resulted from the mixture with citric acid.

Evidence is not conclusive that any of the currently available tetracycline preparations produce any clinically important enhancement of absorption or activity under the conditions usually encountered in treatment.

Kunin, C. M., *New England J. Med.*, 259:147-156, 1958.

Strokes and Anticoagulants

Anticoagulant therapy has dissipated the air of hopelessness that has long surrounded the occurrence of stroke. It is beginning to be accepted for the treatment of transient strokes due to spasm or transient

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1. Levy, S., *J.A.M.A.*,153:1260,1953
2. Thompson L., Procter, R., *North Carolina M. J.*, 15:596,1954
3. Thompson, L., Procter, R., *Clin. Med.* 3:325,1956

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closure of the carotid or basilar-vertebral arteries. The diagnosis is not simple. There is usually a history of transient episodes of numbness and weakness of the face or an arm or leg or of temporary visual disturbances. If the trouble is in one carotid artery, the signs will recur on the same side of the body, unless the other carotid becomes involved. If the closure is in the basilar-vertebral artery and there are multiple attacks, the signs frequently shift from side to side. Some such patients have been labeled neurotics because of the shifting of the signs. They are in grave danger and require immediate anticoagulant therapy.

Strokes with disease of the middle cerebral and other arteries in that area of the brain produce an ischemic infarction with hemorrhage in the acute phase, which contraindicates the use of anticoagulants. Without anticoagulant treatment, patients who have had a stroke run a 25 per cent chance of having another within a year, and a 55 per cent chance of some other kind of thromboembolic episode. The chances of additional episodes within two years are still more formidable. Anticoagulant drugs reduce the risk of releasing additional emboli or propagating a primary clot. They are especially useful in treating strokes due to emboli arising from heart disease—from a mother clot in the heart, the aorta or carotid arteries.

In acute stroke, anticoagulants are to be considered if the spinal fluid shows no indication of bleeding and there is no other evidence of hemorrhage anywhere, and if the blood pressure is normal, subnormal or only slightly elevated and the eye grounds show no sign of increase of intracranial pressure.

Wright, I. S., *Medical News*, 4:1-4, 1958.

Verac

"...in the management of atonic constipation in the aged patient particularly, Veracolate appears to represent a valuable adjunct."*

*Coodley, E.: Clin. Med. 4:1509, (Dec.) 1957

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Antibiotics Annual 1957-1958

edited by Henry Welch, Ph.D., and Felix Marti-Ibanez, M.D. Medical Encyclopedia, Inc., New York, New York. 1958. $12.00

Here are recorded the proceedings of the Fifth Annual Symposium on Antibiotics, all the way from Opening Remarks. There are more than 1,000 pages of it, every page valuable. The book does not lend itself to review. It contains everything any doctor will need to know about antibiotics, in practice or for review, indeed all that is known today on this subject of primary importance.

Clinical Radiology of Acute Abdominal Disorders

by Bernard S. Epstein, M.D., The Long Island Jewish Hospital and Albert Einstein College of Medicine, Yeshiva University, New York City, with 406 illustrations on 224 figures. Lea & Febiger, Philadelphia, Penn. 1958. $15.00

The thought responsible for this work was one of correlating the radiologic manifestations in acute diseases of abdominal organs with clinical symptoms and pathological processes. The text has been kept to a minimum and references to the literature are few. After each section articles considered worthy of review are listed. The text is composed of observations and deductions of many workers—teachers, colleagues and house officers—whose contributions have been of the greatest value. The excellent illustrations are largely the author's own. The book should serve its purpose admirably.

Ciba Foundation Colloquia on Endocrinology, Vol. 12: Hormone Production in Endocrine Tumors

Editors for the Ciba Foundation, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch.; and Maeve O'Connor, B.A. 58 illustrations and cumulative index to Volumes 1-12. Little, Brown & Company, Boston, Massachusetts. 1958. $9.00

From this presentation of work in a highly specialized field, the general practitioner and other clinicians may abstract much of value in recognizing and dealing with a number of rarely encountered pathological conditions.

A Doctor Speaks His Mind

by Roger I. Lee, M.D. Little, Brown & Company, Boston & Toronto. 1958. $3.00

An entertaining volume from which many a doctor may obtain much of pleasure and not a little of wisdom.

Obstetrics and Gynecology

by J. Robert Willson, M.D.; Clayton T. Beecham, M.D.; Isador Forman, M.D.; and Elsie Reid Carrington, M.D.; Temple University School of Medicine. 267 illustrations. The C. V. Mosby Company, St. Louis, Missouri. 1958. $10.75

This textbook is an evolutionary product of a mimeographed summary of the contents of the courses in obstetrics and gynecology as taught the third and fourth year students in the School of Medicine of Temple University. A middle ground is taken between too-concise presentation of the subject on the one hand, and costly, voluminous texts on the other, the idea being to prepare a textbook placing emphasis on changes produced in body structures and their functions by various obstetric and gynecologic conditions, their diagnosis and treatment, suited to the needs of family physician and specialists. Anatomic description and details of diagnostic and surgical procedures of a highly specialized nature are omitted, only the indication for these operations and their contraindications being discussed. The book is a practical, helpful presentation of the subject.

The Physiology and Pathology of The Cerebellum

by Robert Stone Dow, M.D., Ph.D., University of Oregon Medical School; and Giuseppe Moruzzi, M.D., Institute of Physiology, University of Pisa. The University of Minnesota Press, Minneapolis, Minnesota. 1958. $12.50

Increase of knowledge of the cerebellar physiology, made possible by electrical recording methods over the past 20 years, has been stupendous. In this volume the first attempt is made to correlate this new information with facts derived from older investigative methods. It being manifestly impossible to cover completely the pathology of the cerebellum in half of any volume of ordinary size, it was soon decided to give two-thirds of the space to physiology and to deal with clinical symptomatology and pathology less completely. This clinical part, of most interest and use to doctors in practice, in its first chapters approaches the symptomatology of cerebellar deficiency from a physiological point of view. In the systematic review of the various pathological processes affecting the cerebellum, most attention is paid to clinical findings in the various disease processes. It would seem that this is a work unique in the completeness of its presentation of diseases of the cerebellum.

An Atlas of Esophageal Motility in Health and Disease

by Charles F. Code, M.D., Ph.D.; Brian Creamer, M.D., M.R.C.P.; Jerry F. Schlegel, B.S.; Arthur M. Olsen, M.D., M.S.; F. Edmund Donoghue, M.D.; and Howard A. Andersen, M.D., M.S. Mayo Clinic and Foundation. Charles C. Thomas, Springfield, Illinois. 1958. $8.50

The esophagus is a much neglected organ. The more frequent use of studies described in this Atlas would contribute materially to improvements in diagnosis, and the lowering of the death rate. The illustrations so well supplement the text as to make the volume one of the highest teaching value.

Emergency Treatment and Management, Second Edition

by Thomas Flint, Jr., M.D., Permanente Medical Group, Oakland and Richmond, California. W. B. Saunders Company, Philadelphia & London. 1958. $8.00

The newer and more effective methods of treatment that have been perfected in the last four years are given special attention. Important among these are the treatment of barbiturate overdosage, heart arrest, injuries by cold, diving injuries, shock that is vasopressor-resistant, and arterial damage. Increasing use of *Nalline* in determining narcotic addiction, and a blood test available for alcohol intoxication have had results which warrant their inclusion. The section on Pediatric Emergencies has been greatly expanded. The whole book is well worthy of succession to the place made for itself by the first edition.

Intracardiac Phenomena In Right and Left Heart Catheterization

by Aldo A. Luisada, M.D., The Chicago Medical School; and Chi Kong Liu, M.D., The Chicago Medical School. Second edition, revised and enlarged, of Cardiac Pressures and Pulses. Grune and Stratton, New York & London. 1958. $9.50

The right side of the heart was first catheterized in 1930. This method and its revelations were duly recorded in the first edition. Catheterization of the left side of the heart is one of the developments necessitating this second edition. The latter procedure, as applied in the laboratory of the authors since 1956, is now presented in original documents. The scope of the book has been extended to include results obtained through use of intracardiac phonocardiograms and electrocardiograms recorded for the past two years. Other technical details have been included to save the reader the necessity of consulting other works.

Doctor Squibb: The Life and Times of a Rugged Idealist

by Lawrence G. Blochman, Simon & Schuster, New York, New York. 1958. $5.00

When I entered on the study of medicine 55 years ago, chloroform was still popular as an anesthetic, and Squibb's Chloroform enjoyed the reputation of being the best cholorform to be had. That was the introduction of students of that period to Edward Robinson Squibb. We later learned a good deal more about Dr. Squibb, but it is unlikely that graduates in medicine in the past 30 years have learned much about him.